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ESTIVOAUTUMNAL (PLASMODIUM FALCIPARUM) MALARIA

A Survey of Four Hundred and Ninety-Three Cases of Infection with Plasmodium Falciparum in Children

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ON the Isthmus of Panama one meets nearly all the medical problems encountered in temperate zones, although there are noticeable differences in the frequency of their occurrence, due chiefly to variations in climatic conditions, mode of living and degree of development of sanitation. These differences are evident in the treatment of children; one cannot practice pediatrics in Panama without being impressed by the frequency of the malarial fevers and intestinal helminthiasis. These infections are so prevalent that instead of being matters of minor medical importance, as they are in most parts of the United States, they are of prime clinical significance. Studies of helminthiasis and malaria as these conditions manifest themselves on the Isthmus of Panama were undertaken. Reports dealing with the common intestinal parasites encountered here have been published elsewhere.[1]

Relatively little of the extensive literature on malaria deals with the disease as it occurs in children. In some of these reports, the malarial fevers in children have been described in such a way as to suggest that they resemble the malarial fevers as seen in adults. This has not been borne out by clinical observation. Existing misconceptions concerning the incidence, clinical manifestations and treatment of malaria in children prompted this survey.

SOURCE OF MATERIAL

This study was one of three surveys based on investigations of patients with malaria admitted to the pediatric wards of Gorgas Hospital, Ancon, and Colon Hospital, Cristobal, Canal Zone, between July 1,

From the Pediatric Services, Gorgas Hospital, Ancon, and Colon Hospital, Cristobal, Canal Zone.

1. Miller, J. F., and Einhorn, N. H.: Oxyuriasis: A Clinical Survey of Two Hundred Consecutive Cases of Infection with Enterobius Vermicularis in Children, Am. J. Dis. Child. **68**:376-381 (Dec.) 1944. Einhorn, N. H.; Miller, J. F., and

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1939 and July 1, 1945. Because of their unique geographic positions, a wealth of clinical material has accumulated in these two hospitals. The patients were divided into four groups as follows: group 1, consisting of 493 children infected with Plasmodium falciparum; group 2, consisting of 334 children infected with Plasmodium vivax; group 3, consisting of 10 children infected with Plasmodium malariae and, group 4, consisting of 8 children with mixed infections. This presentation is limited to a consideration of the first group. Three hundred and thirty-eight children were treated at Gorgas Hospital, and 155 were treated at Colon Hospital.

In the Canal Zone, there exists a system of state medicine among government employees and their families; therefore, no socioeconomic selection of patients was made in this series, and all groups were represented. Racially, the patients were classified as white, Negro and mestizo. The term race as used in this paper connotes a collection of persons with similar antecedents, customs, language and appearance.

MOSQUITOES AND MALARIA

The malarial parasite is usually transmitted to man by the bite of the female anopheline mosquito. Although over two hundred species of Anopheles have been described, Craig and Faust [2] stated that only about sixty species are capable of transmitting human malaria. Relatively few of these are of practical importance as natural vectors of malaria. Strong [3] stated that many factors influence the transmission of malaria by the mosquito. Among these factors, to mention but a few, are temperature, humidity, life span of the mosquito, percentage of infected mosquitoes, length of their flight, their distance from human habitations and their breeding and biting habits.

The species of Anopheles concerned in the transmission of malaria vary greatly from region to region. In the Canal Zone and adjoining unsanitated areas of the Republic of Panama, the following species of

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Whittier, L.: Ascariasis: Clinical Survey of One Hundred and Twenty-Five Cases of Infection with Ascaris Lumbricoides in Children, ibid. **69**:237-246 (April) 1945. Miller, J. F.; Einhorn, N. H., and Whittier, L.: Ancylostomiasis and Strongyloidiasis: A Clinical Survey of Seventy-One Cases of Ancylostomiasis and Eleven Cases of Strongyloidiasis in Children, ibid. **69**:359-365 (June) 1945. Einhorn, N. H.; Miller, J. F., and Whittier, L.: Intestinal Polyparasitism: Clinical Survey of One Hundred and Sixty-One Cases of Infection with Multiple Intestinal Parasites in Children, ibid. **63**:350-358 (June) 1945. Whittier, L.; Einhorn, N. H., and Miller, J. F.: Trichuriasis in Children: A Clinical Survey of Fifty Cases and Reports of Three Cases with Heavy Infection and Striking Clinical Symptoms, ibid. **70**:289-292 (Nov.-Dec.) 1945.

2. Craig, C. F., and Faust, E. C.: Clinical Parasitology, ed. 3, Philadelphia, Lea & Febiger, 1943, p. 565.

3. Strong, R. P.: Stitt's Diagnosis, Prevention and Treatment of Tropical Diseases, ed. 6, Philadelphia, The Blakiston Company, 1943, vol. 1, pp. 44-49.

Anopheles were incriminated by Darling[4] in 1910: Anopheles albimanus; Anopheles tarsimaculatus; Anopheles pseudopunctipennis and Anopheles argyritarsis. In 1935, Rozeboom[5] reported the infection of Anopheles bachmanni with P. vivax and its probable infection with P. falciparum. In 1937, Anopheles punctimacula was added as a sixth potential vector by Simmons.[6] By far the most important vectors have been A. albimanus, A. tarsimaculatus and A. pseudopunctipennis. A. albimanus prefers water exposed to sunlight. Although no longer a problem in the sanitated areas, it breeds abundantly in the unsanitated areas in the Canal Zone, especially in the shallow waters along the extensive shore line surrounding Gatun Lake. All parts of the zone may be invaded by mosquitoes which develop in these areas. The number of A. tarsimaculatus, which breeds in the brackish water of tidal swamps, has been reduced by a program of canalization and tidal flooding of breeding places with sea water. A. punctimacula is one of the commoner anophelines of the zone and continues to breed throughout the year in shaded pools and streams in unsanitated areas.

EPIDEMIOLOGIC FACTORS

Season.—The Canal Zone is located between latitude 8° 50′ and 9° 25′ north and between longitude 79° 30′ and 80° 5′ west. The climate is tropical, with high humidity, heavy rainfall, a short dry season, lasting from January through April, and a long wet season, lasting from May through December. On the Pacific side, where Gorgas Hospital is located, the average yearly maximum temperature is 87.3 F.; the average yearly minimum temperature is 73 F. The average relative humidity is 83 per cent.[7] The yearly rainfall is not equal in all parts of the Canal Zone. On the Atlantic side, where Colon Hospital is located, precipitation is about twice as much as that on the Pacific side. Vegetation is dense and luxuriant. The terrain is hilly and mountainous in some parts, and numerous streams of various size are present.

4. Darling, S. T.: Studies in Relation to Malaria, Report of the Laboratory of the Board of Health, Department of Sanitation, Isthmian Canal Commission, Mount Hope, Canal Zone, Isthmian Canal Commission Press, 1910.

5. Rozeboom, L. E.: Infection of Anopheles Bachmanni, Petrocchi, with Plasmodium Vivax, Grassi and Feletti, and Observations on the Bionomics of the Mosquito, Am. J. Trop. Med. **15**:521-528 (Sept.) 1935.

6. Simmons, J. S.: Observations on the Importance of Anopheles Punctimacula as a Malaria Vector in Panama, and a Report of Experimental Infection in Anopheles Neomaculipalpus, Anopheles Apicimacula and Anopheles Eiseni, Am. J. Trop. Med. **17**:191-212 (March) 1937.

7. Annual Meteorological Reports, Panama Canal, Department of Operation and Maintenance, Section of Surveys, Mount Hope, Canal Zone, Panama Canal Press, 1939-1945.

The mosquito fauna include about one hundred and twenty-five species and represent all the genera typical of tropical America. Breeding seems to continue throughout the entire year, although in most localities it is reduced during the height of the dry season. In some districts, during the height of the rainy season the streams are full, rapid and prone to floods, thus offering little opportunity for propagation of mosquitoes. However, when the change of season occurs and during the dry season, many streams become nothing more than pools or collections of stagnant water. As such, they are ideal breeding places for mosquitoes and constitute a serious menace to people living in the vicinity.

In this study the number of cases varied from year to year and from month to month. The largest numbers of cases were seen in 1940, 1942 and 1944; the smallest number was seen in 1943 (table 1). There was only one month in the period of six years covered by this survey in

TABLE 1.—*Incidence of P. Falciparum Malaria*

	Month												
Year	Jan.	Feb.	Mar.	Apr.	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Total
1939.....	..	..	..	..	..	..	7	3	8	16	15	11	60
1940.....	15	15	6	7	4	2	9	8	7	4	8	5	90
1941.....	4	5	2	1	1	7	6	1	9	6	4	13	59
1942.....	3	5	0	6	14	11	14	7	9	4	2	12	87
1943.....	6	1	2	3	6	3	5	3	3	3	3	3	41
1944.....	1	1	8	5	13	11	13	14	11	7	5	9	98
1945.....	8	8	12	6	13	11	..	..	..	..	..	..	58
Total....	37	35	30	28	51	45	54	36	47	40	37	53	493

which no cases occurred. The smallest number of cases was observed during the dry season, extending from January through April, while the largest number was observed at the beginning and end of the rainy season, during the months of May, July and December (chart 1). The months of May and December marked the beginning and end of the rainy season, when the small amount of precipitation was sufficient to create puddles of water, which provided excellent breeding places for anopheline mosquitoes.

Location and Character of Dwellings.—From the point of view of sanitation, communities on the Isthmus of Panama are considered as being (1) sanitated, (2) partially sanitated or (3) unsanitated. It was observed that the number of children in whom malaria developed in partially sanitated areas was almost as large as the number in whom it developed in completely unsanitated areas. For purposes of this report, therefore, partially sanitated districts were not considered separately and patients who came from either unsanitated or partially sanitated areas were grouped together.

A sanitated community is one in which the following conditions exist: (1) The homes are screened and located a considerable distance from native villages; (2) all mosquitoes on the premises and the breeding places of mosquitoes within 1,000 feet (305 meters) of the premises of the most outlying house are destroyed; (3) all refuse, undergrowth, brushwood and useless receptacles likely to harbor mosquitoes are removed or destroyed; (4) sanitary squads are employed to drain or fill small pools, pour larvicides or oil into larger pools and provide drainage

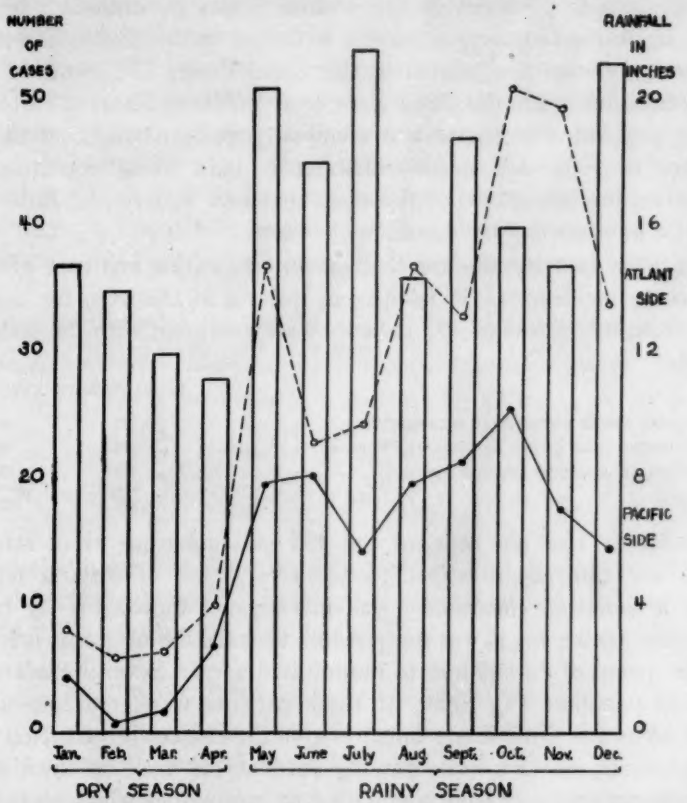

Chart 1.—Seasonal frequency of P. falciparum malaria.

in and for a considerable distance around the community, and (5) all hospital patients with malaria are treated in rooms or wards protected from mosquitoes. Thus sanitation resolved itself into the destruction of the anopheline vectors of malaria and their breeding places, the protection of man from the bites of these vectors and the destruction of Plasmodia in infected persons.

The communities from which the patients came were of three types as follows: (1) United States government communities located in the

Canal Zone, characterized by minimal crowding, excellent facilities for sewage disposal, paved streets, landscaped yards and complete sanitation; (2) principal cities of the Republic of Panama, in the centers of which overcrowding among the poor is commonplace, sewage disposal is adequate and streets and alleys are paved; in the outskirts of these cities, drainage and sewage disposal facilities are minimal, the streets are unpaved and landscaping is absent; by arrangements by treaty with the Republic of Panama, sanitation in the cities of Colon and Panama is provided by the United States government; in these cities sanitation compares favorably with that in the United States government communities located in the Canal Zone; (3) rural or semirural communities in the Canal Zone or Republic of Panama (interior), where population is sparse and frequently gathered together in small villages of from 50 to 200 inhabitants; here living conditions are primitive, the homes are of the open thatched variety and little or no attempt at screening or sanitation is made.

In order to determine the relationship of location and type of dwelling to the incidence of P. falciparum malaria in children, the available data from this series of 493 patients were analyzed, with the following results:

	No. of Patients	Per Cent
United States government communities	42	8.5
Principal cities of the Republic of Panama	33	6.7
Rural or semirural communities	418	84.8
Total	493	100.0

That 75, or 15.2 per cent, of the 493 patients came from sanitated areas was contrary to expectations. Every case of malaria reported from a sanitated community was investigated thoroughly by trained workers. However, it was not possible to trace the origin of infections in this group of 75 children to unsanitated areas. Several explanations seemed possible: (1) Some of these patients wandered into unsanitated areas and unwittingly failed to give the correct information to the investigators, or (2) while playing outdoors at dusk or dawn certain of these patients may have been bitten by mosquitoes which were blown in from adjoining unsanitated areas. The 493 patients with P. falciparum malaria named one hundred communities as their homes. Two hundred and twenty-nine, or 46.5 per cent, of patients came from ten, or 10 per cent, of the communities and villages named. Sixty-two, or 12.6 per cent, came from the native village of Chilibre, and 44, or 8.9 per cent, came from the village of Chiva Chiva, indicating that some areas are more definitely reservoirs of infection than others.

Age.—The age distribution is shown in table 2. The youngest patient in this study was a 5 week old infant. There were 4 infants under 2 months. Thirty-seven, or 7.5 per cent, had had their first attack by the

end of their first year of life, and an additional 61, or 12.4 per cent, had had their first attack by the end of the second year. Thus, by the end of the second year of life 19.9 per cent, or approximately one-fifth of the children, had had at least one attack of P. falciparum malaria. From the age of 2 to 12 years the incidence per year of life was uniformly high.

Sex.—Two hundred and seventy-six, or 56 per cent, were boys and 217, or 44 per cent, girls (table 2).

Race.—Striking differences in racial distribution were observed. Three hundred and seventy-five of the patients, or 76 per cent, were mestizo; 96, or 19.5 per cent, were Negro, and 22, or 4.5 per cent, were white. These pronounced differences were closely related to the habitations of the patients. A few of the mestizo and all the white patients lived where sanitation was entirely satisfactory. Many of the Negroes lived where sanitation and environmental factors were only fairly satisfactory. A few of the Negro as well as most of the mestizo children actually lived on the soil, in thatched and unscreened huts located

TABLE 2.—*Distribution of 493 Children with P. Falciparum Malaria, According to Age and Sex*

Age, Yr.	3/12	6/12	9/12	1	1 3/12	1 6/12	2	3	4	5	6	7	8	9	10	11	12	Total
Males	3	1	4	13	3	12	17	27	22	26	17	17	27	23	29	16	19	276
Females	2	2	5	7	4	10	15	17	16	20	15	17	17	21	10	16	23	217
Total	5	3	9	20	7	22	32	44	38	46	32	34	44	44	39	32	42	493

in completely unsanitated areas. Fourteen, or 63.6 per cent, of the 22 white children acquired P. falciparum malaria after a single vacation trip into the interior of the Republic of Panama.

SYMPTOMATOLOGY OF P. FALCIPARUM MALARIA

The following questions were answered carefully before the symptoms and physical signs presented by each child were analyzed: Was the present attack of malaria the first attack; if not, when and of what type was the last attack and were any of the symptoms observed due to the presence of associated unrelated diseases? In order to answer the questions relating to the number of attacks experienced by each child, the 493 cases of P. falciparum malaria were classified into four groups as follows: (1) primary malaria, (2) questionable primary malaria, (3) recurrent malaria and (4) questionable recurrent malaria.

One hundred and sixty-six patients with primary malaria satisfied three or more of the following criteria: (1) no history of a previous attack of malaria, (2) residence either in a sanitated area or for less than six weeks in an unsanitated area, (3) no history of a recent trip

into an unsanitated area and (4) absence of physical signs attributable to a previous attack of malaria.

Fifty-nine patients with questionable primary malaria satisfied two or more of the following criteria: (1) no history of a previous attack of malaria; (2) prolonged residence in an unsanitated area, indicating the possibility of previous or constant exposure to malarial infection, and (3) absence of physical signs attributable to a previous attack of malaria.

One hundred and twenty patients with recurrent malaria satisfied one of the following criteria: (1) presence of a definite history of a previous attack of malaria within a period of less than one year without new exposure or (2) history of either a previous attack of malaria or bouts of fever of undertermined origin within a period of over one year with physical signs attributable to a previous attack of malaria.

TABLE 3.—*Associated Unrelated Diseases in 493 Children with P. Falciparm Malaria*

Disease		Number of Patients
Intestinal helminthiasis		186
Disease of the respiratory tract		7
Rhinopharyngitis	3	
Pneumonia	2	
Asthma	1	
Otitis media	1	
Acute communicable disease		3
Bacillary dysentery		2
Surgical conditions		2
Acute glomerulonephritis		1
Miscellaneous		3
Total		204
P. falciparum malaria, unassociated		289

One hundred and forty-eight patients with questionable recurrent malaria satisfied one or more of the following criteria: (1) history of a previous attack of malaria or of frequent bouts of fever of undetermined origin, with or without a history of response to antimalarial therapy; (2) no definite history of a previous attack of malaria in a patient whose prolonged residence in an unsanitated area indicated the probability of previous or constant exposure to malarial infection, and (3) presence of physical signs attributable to a previous attack of malaria.

Two hundred and four children, or 41.4 per cent, had conditions in addition to malaria, and 289, or 58.6 per cent, had symptoms accounted for by malaria alone (table 3). Of the unrelated associated diseases encountered, infection with intestinal parasites and miscellaneous conditions of the respiratory tract were most frequent, with totals of 186 patients (37.7 per cent) and 7 patients (1.4 per cent) respectively.

The helminths commonly observed were Ascaris lumbricoides, Trichuris trichiura, Strongyloides stercoralis and the hookworms.

Symptoms were divided into three classes as follows: (1) those presumably due to malaria. (2) those due to either malaria or associated unrelated disease and (3) those due to associated unrelated disease. Symptoms which could not be explained completely by the unrelated disease were listed under malaria. The third group included such complaints as cutaneous rash, otorrhea, rhinorrhea and sore throat. This aggregate seemed to bear no obvious relation to P. falciparum malaria; hence it was eliminated from consideration. The second group—those attributable to either malaria or associated unrelated disease—could not be eliminated without the introduction of the possibility of discarding important and relevant findings. It seemed reasonable, therefore, to

TABLE 4.—*Symptomatology of P. Falciparum Malaria*

	Type of Malaria									
	Primary		Questionable Primary		Recurrent		Questionable Recurrent		Total	
Symptoms	No.	%	No.	%	No.	%	No.	%	No.	%
Chills and fever	69	41.6	36	61.0	66	55.0	86	58.1	257	52.1
Vomiting	80	48.2	29	49.2	61	50.8	73	49.3	243	49.3
Fever	96	57.8	22	37.3	52	43.3	60	40.5	230	46.7
Headache	53	31.9	24	40.7	35	29.2	50	33.8	162	32.9
Anorexia	52	31.3	21	35.6	35	29.2	45	30.4	153	31.0
Cough	52	31.3	11	18.6	28	23.3	28	18.9	119	24.1
Somatic pain	29	17.5	10	16.9	15	12.5	25	16.9	79	16.0
Abdominal pain	14	8.4	3	5.1	22	18.3	21	14.2	60	12.2
Delirium	24	14.5	5	8.5	5	4.2	11	7.4	45	9.1
Convulsions	22	13.3	7	11.9	8	6.7	4	2.7	41	8.3
Diarrhea	18	10.8	1	1.7	10	8.3	12	8.1	41	8.3
Fretfulness, irritability, restlessness	10	6.0	3	5.1	3	2.5	8	5.4	24	4.9
Drowsiness, listlessness	10	6.0	0	0.0	1	0.8	2	1.4	13	2.6
Sweats	4	2.4	1	1.7	6	5.0	0	0.0	11	2.2
Weakness	2	1.2	5	8.5	3	2.5	1	0.7	11	2.2
Constipation	3	1.8	1	1.7	1	0.8	4	2.7	9	1.8
Epistaxis	1	0.6	1	1.7	1	0.8	4	2.7	7	1.4
Loss of or failure to gain weight	1	0.6	0	0.0	4	3.3	0	0.0	5	1.0
Pain in chest	0	0.0	0	0.0	1	0.8	3	2.0	4	0.8
Dizziness, syncope	1	0.6	1	1.7	0	0.0	0	0.0	2	0.4
Dyspnea	1	0.6	0	0.0	1	0.8	0	0.0	2	0.4
Jaundice	1	0.6	0	0.0	0	0.0	0	0.0	1	0.2

combine this second group with the groups of symptoms presumed to be due to P. falciparum malaria (table 4). By that procedure it was hoped to obtain a more accurate index of the symptoms of P. falciparum malaria.

The textbook description of the onset of an attack of malaria consists of a chill, fever and prostration. The typical paroxysm consists of the classic chill, fever and sweat, or the "cold," "hot" and "sweating stages." However, the mode of onset and the character of the paroxysms observed in this survey followed a more irregular pattern. Prodromal symptoms such as anorexia, drowsiness, fretfulness, headache, irritability and muscular and somatic pains were observed frequently before the

onset of the first paroxysm. This type of onset was commoner than the sudden onset, with chill, fever and prostration. The cold, hot and sweating stages were not distinct, and the symptoms characteristic of one stage were often observed in other stages of the paroxysm.

Cold Stage.—All the temperatures recorded in this study were taken rectally. Chills and fever, vomiting, and fever alone were the most frequent symptoms, occurring in 52.1, 49.3 and 46.7 per cent of the patients respectively. Thus fever was the commonest finding, having been observed in 98.8 per cent of the patients. The associated chill, which was absent in slightly less than one half of the patients, seemed to be replaced frequently by such symptoms as convulsions or vomiting followed by fever. Patients oftener complained of a feeling of chilliness and of cold extremities rather than a definite chill. When a chill was present the child complained of feeling cold. The face, lips, hands and feet were cold and cyanotic. The pulse was rapid, weak and often irregular. The temperature rose gradually and varied from 101 F. to a high of 108.2 F. The average maximum temperatures in primary and recurrent P. falciparum malaria were 103.2 and 101.8 F. respectively. The cold stage lasted approximately two hours and was followed by the hot stage. Vomiting, however, persisted for from twelve to twenty-four hours and in a few instances continued as long as ninety-six hours.

Hot Stage.—During the hot stage of the paroxysm, the face was congested and the skin of the entire body surface became flushed and hot. The pulse was rapid, full and often irregular. Typically in older children the temperature rose rapidly during the hot stage. This first rise was followed by a slight drop and a secondary rise, which reached as high as or even higher than the first elevation, after which the temperature returned to normal. More frequently, however, the temperature curves were decidedly irregular, and fevers persisted for from four to thirty-six hours before definite drops occurred. In this stage were observed the pronounced symptoms referable to the central nervous system. Delirium occurred in 45 (9.1 per cent), convulsions in 41 (8.3 per cent) and coma in 24 (4.9 per cent). These symptoms were more frequent in primary than in recurrent P. falciparum malaria. Delirium, stupor and coma when present were pronounced and in a number of instances were associated with convulsions. Of the 41 children who had convulsions, 10 had such associated conditions as intestinal helminthiasis, bacillary dysentery and pneumonia. Although the convulsions might have been caused either by the malarial infections or by the associated unrelated diseases, the available evidence favored the former origin. When the mentality was clear, complaints of headache, abdominal pain and aching of the muscles of the extremities were frequent. Cough, vomiting and diarrhea were commonly observed during the hot stage.

Sweating Stage.—The sweating stage was not often clearly differentiated. Fever subsided rapidly once it started to fall, although symptoms disappeared slowly. Patients did not experience a feeling of well-being during apyrexial periods as they did in other forms of malaria.

Craig [8] has divided the fever observed in malaria into five stages: the initial rise, the stage of oscillation, the pseudocrisis, the precritical rise and the true crisis. The temperature curves, particularly those observed in children under 4 years, were not so typical as might be gathered from standard textbooks. For most of the patients, the diagnosis was established and treatment started shortly after admission to the hospital, so that there was little opportunity to observe the course of the temperature in untreated patients. However, for various reasons, the diagnosis was delayed in 23 cases. The temperatures in this small group often followed an atypical course. These irregular or more or less continuous temperature curves may have been due to the presence of two or more generations of P. falciparum segmenting at different times.

Anorexia, vomiting, abdominal pain and diarrhea were frequent during the cold and hot stages. One hundred and eighty-six, or 37.7 per cent, of the 493 patients were infected with intestinal parasites. Although these symptoms were common in helminthiasis, the frequency with which they were observed in the latter was not so great as their frequency in malaria.[1] As soon as the malarial infection was brought under control, the gastrointestinal symptoms disappeared. It seemed reasonable, therefore, to assume that the malarial rather than the helminthic infections were more directly concerned in their causation.

The term pernicious malaria has been applied to any type of malaria in which the symptoms are of a serious or grave character, particularly that due to P. falciparum. Such descriptive terms as cerebral, gastralgic, algid, bilious remittent and hemorrhagic have been applied to severe or pernicious malaria. However, these are descriptive terms, and they refer to symptoms which depend mainly on the localization of sporulating parasites in internal organs and not to particular disease entities. The cerebral and algid forms were the commonest forms of pernicious malaria observed in this study.

Cerebral Form.—The cerebral form was characterized by coma, which came on suddenly or developed gradually after a period, of variable duration, of drowsiness, restlessness, muscular twitchings, delirium, stupor and convulsions. The sudden type of onset was observed in 1 child who had a single convulsion at school and was brought to the hospital in coma shortly thereafter. In 31 others, who had the

8. Craig, C. F.: The Malarial Fevers, in Brennemann, J.: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., 1945, vol. 2, chap. 10, p. 16.

cerebral form of malaria, the onset was more gradual. Temperature of 106 F. or over was present in 14 of these patients. In 1 child, who recovered, the temperature reached 108.2 F.

The following is a typical history in a case of the cerebral form of P. falciparum malaria:

CASE 1.—A 9 year old Negro boy was admitted with the complaints of chills and fever of seven days' duration and coma of eight hours' duration. The child had had an attack of P. falciparum malaria three months previously. He had lived in an unsanitated area since birth.

Physical Examination.—The boy was acutely ill and in deep coma. He was fairly well nourished and weighed 55 pounds (24.9 Kg.). The temperature was 103 F.; the respiratory rate was 28, and the pulse was rapid and weak. The lips and lobes of the ears were slightly cyanotic; the skin was hot to the touch; the liver and the spleen were not palpable. Moderate nuchal rigidity was present; a Kernig sign was not present.

Laboratory Examination.—The hemoglobin concentration was 60 per cent (Tallqvist); there were 3,200,000 erythrocytes, 11,600 leukocytes, 82 per cent neutrophils and 18 per cent lymphocytes. Blood smears were positive for P. falciparum. The urine was normal. The stool was negative for parasitic ova and Endamoeba histolytica. The cerebrospinal fluid was clear, and there were 2 cells per cubic millimeter. A Kahn test of the blood gave a negative reaction.

Treatment and Course.—On admission to the hospital, the patient was given an intramuscular injection of 0.2 Gm. of quinacrine hydrochloride (atabrine). This treatment was repeated in six hours. The drug was then administered orally in doses of 0.1 Gm. three times a day for six successive days. The first few oral doses were administered by means of a small catheter passed through the nose into the stomach. Two intravenous injections of 5 per cent dextrose in isotonic solution of three chlorides (Ringer's solution) were administered during the first forty-eight hours. Barbiturates were given when necessary for sedation.

The patient was comatose and had fourteen convulsions during the first forty-eight hours of his illness in the hospital. The temperature ranged from 98 to 104 F. for three days. On the fourth day the child was in a stupor. On the fifth day he seemed to be disoriented, but from then on recovery was rapid. Plasmodia disappeared from the peripheral blood on the fourth day.

Algid Form.—The algid form of P. falciparum malaria was characterized by symptoms and signs of collapse. It was observed in 1 child with primary and 6 with recurrent malaria. These children had from one to four paroxysms at home before being brought to the hospital, although 2 of them collapsed after admission to the hospital. The symptoms developed during or shortly after a chill and consisted in pallor, cold and clammy skin, rapid and weak pulse, muscular weakness and stupor.

The following is a typical history in a case of the algid form of P. falciparum malaria:

CASE 2.—A 9 year old mestizo girl was admitted with the complaints of fever, of three days' duration, and headache and inability to talk, of one day's duration. There was no history of a previous attack of malaria. The patient had lived in an unsanitated area since birth.

Physical Examination.—The girl was acutely ill and in a stupor. She was fairly well nourished and weighed 52 pounds (23.6 Kg.). The temperature was 106.4 F.; the respiratory rate was 30; the pulse was rapid and weak, and slight cyanosis of the lips was present The blood pressure was recorded as 114 systolic and 62 diastolic. The skin was cold and clammy, the abdomen was distended, the spleen was firm and palpable 2 cm. below the left costal margin and a Kernig sign was not present.

Laboratory Examination.—The hemoglobin concentration was 78 per cent (Sahli); there were 4,500,000 erythrocytes, 5,600 leukocytes, 77 per cent neutrophils, 18 per cent lymphocytes and 5 per cent monocytes. Blood smears were positive for P. falciparum. The urine contained a trace of albumin and an occasional granular cast. A Kahn test of the blood gave a negative reaction. Cultures of the stools yielded no pathogens. The stool was positive for ova of Necator americanus and T. trichiura, but no amebas were found. The cerebrospinal fluid was clear, and there were 6 cells per cubic millimeter.

Treatment and Course.—On admission to the hospital, the patient was given an intramuscular injection of 0.2 Gm. of quinacrine hydrochloride. This treatment was repeated in six and again in twelve hours. The drug was then administered in doses of 0.1 Gm. three times a day for six successive days. The first few oral

TABLE 5.—*Physical Findings in P. Falciparum Malaria*

Physical Findings	Type of Malaria							
	Primary		Questionable Primary		Recurrent		Questionable Recurrent	
	No.	%	No.	%	No.	%	No.	%
Liver and spleen not palpable	163	98.2	54	91.5	20	16.7	42	28.4
Spleen palpable	0	0.0	0	0.0	79	65.8	71	48.0
Liver palpable	3	1.8	4	6.8	0	0.0	5	3.4
Liver and spleen palpable	0	0.0	1	1.7	21	17.5	30	20.3

doses were administered by means of a small catheter passed through the nose into the stomach. The patient was given three intravenous injections of 5 per cent dextrose in isotonic solution of three chlorides during the first seventy-two hours. Barbiturates were administered as necessary for sedation. Later tetrachloroethylene was used in the treatment of the hookworm infection.

The patient remained in a stupor for ninety-six hours. She moaned almost incessantly and held her abdomen with her hands, as if in pain. The latter was so obvious that considerable concern about the presence of an acute condition within the abdomen was expressed. Persistent vomiting was present on the first day. The temperature ranged from 98.2 to 106 F. for four days and returned to normal on the sixth day. The patient became somewhat rational on the fourth day but continued to be disoriented for another day. From then on recovery was rapid. Plasmodia disappeared from the peripheral blood on the fourth day.

PHYSICAL FINDINGS

Abnormal physical signs were not numerous. Pallor was frequent. Stupor, delirium, coma and sweats have been described under symptoms. The most important physical findings were those in connection with the liver and spleen (table 5). The spleen was not palpable in primary or questionable primary P. falciparum malaria, although it was ques-

tionably palpable in several patients who had experienced two or more paroxysms before entrance into the hospital. The spleen was palpable in 83.3 per cent and the liver was palpable in 17.5 per cent of the patients with recurrent malaria. Neither the liver nor the spleen was palpable in 16.7 per cent of the patients with recurrent and 28.4 per cent of those with questionable recurrent malaria. When palpable these organs were usually firm. The edge of the liver extended from 1 to 4 cm. below the right costal margin. The edge of the spleen extended from 1 cm. below the left costal margin to the crest of the ileum. In the 268 patients with recurrent or questionable recurrent malaria the spleen extended to the umbilicus in 94 and to the crest of the ileum in 7. Abdominal enlargement was usually associated with the splenomegaly and hepatomegaly.

Many of the children with recurrent malaria were underweight. The heights and other measurements were not known, as these figures were not obtained routinely in the pediatric service. In spite of this deficiency, it is possible to make the general statement that underweight

TABLE 6.—*Nutritional State of Children with P. Falciparum Malaria*

State of Nutrition	Primary		Questionable Primary		Recurrent		Questionable Recurrent	
	No.	%	No.	%	No.	%	No.	%
Poor	24	14.5	13	22.0	48	40.0	59	39.9
Fair	32	19.3	16	27.1	22	18.3	35	23.6
Good	110	66.3	30	50.8	50	41.7	54	36.5

was a common finding, particularly among the younger children. The normal weights given by Griffith and Mitchell [9] were used as standards. Any weight within plus or minus 7 per cent of these weights was considered within the normal range. Children whose weights were 7 to 14 per cent below normal were considered as being fairly well nourished, and those whose weights were more than 14 per cent below normal were considered as being poorly nourished. The results of this analysis are presented in table 6. Poor nutrition was approximately three times as frequent in recurrent as in primary malaria. The percentage of fairly well nourished children was approximately the same in all groups. The largest number of well nourished children was observed in primary malaria.

LABORATORY DATA

Hemoglobin Determinations.—Estimations made by the Tallqvist technic were available for the entire group of 493 patients. When the concentration of hemoglobin was found to be below 50 per cent, the

9. Griffith, J. P. C., and Mitchell, A. G.: Textbook of Pediatrics, ed. 3, Philadelphia, W. B. Saunders Company, 1941, pp. 4-5.

result was checked by the Sahli method. The values obtained are given in tables 7 and 8. The average percentage of hemoglobin was 62.5 This value compared favorably with that observed in a group of children admitted to the surgical service with simple uncomplicated fractures and free from medical disease. Two hundred and three patients (41.2 per cent) had hemoglobin levels of 60 per cent or less, and in 67

TABLE 7.—*Average Erythrocyte, Leukocyte and Differential Counts; Concentrations of Hemoglobin and Number of Days Parasites Persisted in Children with P. Falciparum Malaria*

Type of Malaria	Primary	Questionable Primary	Recurrent	Questionable Recurrent	General Average
Hemoglobin, per cent.....	63.8	63.0	63.0	61.0	62.5
Erythrocytes, million.....	3.6	3.3	3.5	3.5	3.5
Leukocytes, thousand.....	7.7	7.9	7.8	8.1	7.9
Neutrophils, per cent.....	63	60	61	59	61
Lymphocytes, per cent.....	36	38	37	40	38
Eosinophils, per cent.....	1.2	2.2	1.5	1.5	1.4
Persistence of parasites, days	2.6	2	2.3	2.6	2.4

of these (13.6 per cent) the levels were below 50 per cent. Low concentrations were observed in patients who had experienced several paroxysms at home, before entrance into the hospital, as well as in patients with recurrent P. falciparum malaria. One hundred and eighty-six of these patients had intestinal parasites, which may have contributed to the reduction in concentrations of hemoglobin.

TABLE 8.—*Concentration of Hemoglobin in Children with P. Falciparum Malaria*

Hemoglobin, per Cent	Type of Malaria, per Cent of Patients			
	Primary	Questionable Primary	Recurrent	Questionable Recurrent
10	0.0	1.7	0.0	0.0
20	0.0	0.0	0.0	0.0
30	2.4	0.0	0.0	0.7
40	1.2	1.7	1.6	4.7
50	5.4	5.1	10.8	16.1
60	22.2	23.7	36.6	27.7
70	61.4	57.6	43.3	45.2
80	7.2	10.2	7.5	5.4

Erythrocyte Counts.—The patients with erythrocyte counts below 3,200,000 were essentially the same 203 who had low values for hemoglobin. Counts of less than 2,000,000 were recorded in 6 patients, 3 of whom had only P. falciparum malaria and 3 of whom also had intestinal helminthiasis. The greatest reductions in number of erythrocytes were observed in children who had experienced several paroxysms at home, before entering the hospital, as well as in children with recurrent malaria. None of the patients with severe anemia had jaundice. Poikilocytosis

and anisocytosis were observed when the number of erythrocytes dropped below 3,000,000.

Leukocyte Counts.—Although the total number of leukocytes varied from 3,400 to 17,200, the average number was 7,900 (table 7). A total of 283 patients, or 57.4 per cent, had counts below this average. Leukocyte counts above 12,000 were obtained in 47, or 9.5 per cent, of the patients. One of the latter had sickle cell anemia, 1 had acute rhinopharyngitis, 1 had pneumonia, 16 had intestinal helminthiasis and 28 had only P. falciparum malaria.

Differential Leukocyte Counts.—The number of neutrophils varied from a low of 14 per cent to a high of 91 per cent, with an average of 61 per cent. The number of lymphocytes and monocytes combined varied from 7 to 82 per cent, with an average of 38 per cent (table 7). Although the average number of mononuclear leukocytes was only 0.8 per cent, 15 patients had counts greater than 5 per cent and 3 of these had counts between 10 and 14 per cent. The number of basophils was insignificant. The number of eosinophils varied from none to 25 per cent. Todd and Sanford [10] have stated that the maximum normal number of eosinophils is 4 per cent. By this standard, 30, or 6.1 per cent, of the patients had eosinophilia and 463, or 93.9 per cent, did not have this condition. Of the 30 who had eosinophilia, 15 had intestinal helminthiasis.

Kahn and Wassermann Reactions.—Kahn tests were made on 387 patients. These tests were usually made after a good response to antimalarial therapy had been obtained. Positive reactions were obtained in 24, or 6.2 per cent, of those tested. Wassermann tests made on this small group of positive reactors gave positive reactions in most instances. There was no clinical evidence of coincidental syphilis. Only 8 of these children were seen again; negative reactions were obtained in all of them.

Urinary Examinations.—One child had acute glomerulonephritis when admitted to the hospital. As nearly as could be determined he had had at least three paroxysms at home, and slight edema of his face was observed four days prior to his admission to the hospital. The urine of 79, or 16 per cent, of the patients contained albumin and granular casts. Albuminuria was commonest in the cerebral and algid forms of malaria; 34, or 87.2 per cent, of the 39 patients with pernicious malaria presented this finding.

Laboratory Diagnosis of P. Falciparum Malaria.—P. falciparum were demonstrated in the blood films of all the patients studied. Separate

10. Todd, J. C., and Sanford, A. H.: Clinical Diagnosis by Laboratory Methods, ed. 10, Philadelphia, W. B. Saunders Company, 1943, pp. 278-279.

thin and thick films were made on each patient. Thin films were prepared in the usual way, dried in the air and stained with Hastings' stain. The preparations were flooded with the concentrated stain for a few seconds, and an equal amount of water was added by means of a small pipet until a metallic sheen appeared on top of the stain. The dilute stain was allowed to remain on the slide for three minutes and then flushed off with water. The preparation was dried in the air. Thick films were prepared by collecting a large drop of blood on a clean, grease-free slide. The blood was spread over an area of about 1 cm. with the corner of another slide, placed on a flat surface and allowed to dry thoroughly in the air. The slide was then immersed in a freshly prepared solution of 1 part of Giemsa stain to 30 parts of water for thirty-five minutes, washed and dried in the air. This method accomplishes dehemoglobinization and staining. Because it effects a concentration of parasites, it results in a saving of time when large numbers of slides are being examined. However, this staining process may distort the parasites, and it provides no background of erythrocytes on which to see the parasites. Consequently, much more experience is needed in examination of thick preparations than in examination of thin ones.

The differential diagnosis of malarial parasites in blood films depends on the recognition of the differential morphologic features of the various species of malarial Plasmodia. The following features are characteristic of infection with P. falciparum: (1) The young trophozoites are small and occupy one sixth to one fourth of the infected erythrocyte; (2) the infected erythrocytes are never enlarged; they may show single or multiple infection, and the trophozoites appear as fine hairlike rings, with the chromatin in the form of a single bar or two dots; (3) the parasites contain little or no pigment; (4) basophilic granules or Maurer's dots may be present in the cytoplasm of the infected erythrocytes; (5) the number of merozoites varies from 8 to 32 and is usually from 14 to 16; (6) only ring forms, young pigmented forms and gametocytes appear in the peripheral blood; other developmental forms occur in the internal organs and rarely appear in the peripheral blood, and (7) gametocytes are either elliptic or crescentic and often appear in the blood after one week of fever.

Except in cases of fulminating malaria, intermediate forms rarely appeared in the peripheral blood and gametocytes were uncommon. Thus, the diagnosis of P. falciparum malaria was usually made on the observation of young ring forms alone. These forms, which were small, multiple infections of single erythrocytes, were frequent, and the infected erythrocytes were not enlarged. Although this provided only presumptive evidence, experience has shown that over 95 per cent of the diseases diagnosed on the basis of this evidence were P. falciparum

malaria. In the remaining 5 per cent, study of subsequent smears of the blood showed, for example, the presence of a P. vivax trophozoite. In such circumstances there was no hesitancy in changing the diagnosis.

In this series of 493 patients parasites persisted for from one to twelve days, with a median of two and an average of two and two-tenths days. The average in primary malaria was two and six-tenths days and in recurrent malaria two and three-tenths days. Crescent-shaped gametocytes were observed in 73, or 14.8 per cent, of the patients, 10 of whom had primary and 32 recurrent malaria, a ratio of 1 : 3.2. When present, gametocytes persisted for from one to twenty-two days, with an average of six and two-tenths days. Smears were made daily. No patient was discharged from the hospital until three successive smears negative for malarial organisms were obtained.

RELAPSES IN P. FALCIPARUM MALARIA

Relapses occurred in 120, or 24.3 per cent, of the patients. Seventeen had recrudescences within a period of two months; 32 had relapses within periods of from two to six months, and 71 had recurrences within periods of from six to twelve months of the preceding attack. The average interval between periods of renewed activity was slightly less than seven months, the distribution having been as follows:

Months Between Periods of Renewed Activity	Number of Patients	Months Between Periods of Renewed Activity	Number of Patients
1	11	7	6
2	6	8	28
3	12	9	7
4	8	10	12
5	7	11	14
6	5	12	9

The total number of attacks experienced by this group of 120 patients was three hundred and sixteen, an average of 2.6 per child. Eighty-three patients had two attacks, 16 had three, 7 had four, 10 had five and 4 had six. Seven were white children who lived in sanitated areas in the Canal Zone and had acquired their primary infections after single trips into unsanitated areas. Attempts to trace the source of the infection in 3 Negro children living in sanitated areas yielded questionable information. The remaining 110 patients lived in unsanitated areas, and what was called a relapse or period of renewed activity for purposes of this report may have been a reinfection. Because these patients were exposed to infection continuously, the final differentiation between reinfection and relapse could not be made.

Although periods of renewed activity often follow conditions which lower the general resistance of the body, no obvious causes were found in 60 patients. Fifty-seven patients had intestinal helminthiasis, 1 had pneumonia, 1 had an acute rhinopharyngitis and 1 had pertussis.

Latent Malaria.—On the Isthmus of Panama there are numerous regions in which the malarial fevers are highly endemic. Children with persistent malarial infections are encountered frequently in these areas. This type of infection is known as latent infection. The general impression is that latent malaria is a parasitemia without serious clinical manifestations. Such an impression is erroneous. One may divide the patients with malarial infections into two groups: (1) the group that seeks treatment in hospitals and (2) the group that remains at home. The latter are the patients in whom malarial infections are latent and in whom the infections may be as severe as they are in those who are brought to hospitals for treatment. Locally, these children are the inhabitants of the unsanitated areas in the Canal Zone and interior of the Republic of Panama. As a general rule, the native is sick and complains only when he is confined to his hammock. The children are considered as being sick only when they are confined to their hammocks or are otherwise incapacitated by malarial infections. On the other hand, a single chill, a bout of fever or less striking symptoms in a white child will cause his mother to seek medical aid. Latent malaria is malarial infection in the strictest sense. If children with latent infections with P. falciparum were observed over extended periods, it would be seen that their infections during periods of renewed activity do not differ from those observed in hospitals.

Clark [11] demonstrated a high degree of endemicity of malarial infection in the areas from which many of the patients in this survey came. He showed that in villages where the infected natives were treated with either quinacrine hydrochloride or quinine the rate of infection in infants under 1 year was 5.9 per cent. In villages from which the untreated controls came, the rate was 20 per cent. Clark [12] was also able to show that the highest rates of infection occurred in the age group extending from 5 to 20 years. He was of the opinion that the children who harbor parasites in their blood acquire a tolerance which resembles but is not true immunity. In the child who has lived in an endemic area this tolerance is considerable at the age of puberty. However, it is unstable, and as soon as these young persons enter on an active life the fatigue, strain and exposure upset their relatively low degree of immunity. Children with latent infections are usually seriously injured by such infections. Their physical and mental growth is

11. Clark, H. C., and Komp, W. H. W.: A Summary of Ten Years of Observation on Malaria in Panama with Reference to Control with Quinine, Atrabine and Plasmochin, without Anti-Mosquito Measures, in Moulton, F. R.: A Symposium on Human Malaria, Publication 15, American Association for the Advancement of Science, 1941, pp. 273-284.

12. Clark, H. C.: The Age Level for the Peak of Acquired Immunity to Malaria as Reflected by Labor Forces, Am. J. Trop. Med. **24**:159-161 (May) 1944.

retarded, splenic enlargement is pronounced and varying degrees of anemia and underweight are present. Such children are carriers of malaria and are a danger to themselves as well as to other members of the community.

COMPLICATIONS AND SEQUELAE OF P. FALCIPARUM MALARIA

Relatively few complications were observed in the 493 patients with P. falciparum malaria. Bronchopneumonia occurred in 4 patients, acute suppurative otitis media in 4, acute hemorrhagic nephritis in 1, acute psychosis in 1, monoplegia in 1 and paraplegia in 1. One child had bronchopneumonia when he was admitted to the hospital, and the disease developed in another on the fourth day following admission. In 2 patients, bronchopneumonia developed on the ninth and sixtieth days following admission to the hospital. There was no reason to believe that the pneumonia in these particular patients was caused by P. falciparum. Although albuminuria was common, it disappeared by the time the patients recovered from malaria. A 5 year old boy, who had been ill with malaria one week prior to entrance into the hospital, had acute glomerulonephritis and died forty hours after admission. Mental confusion lasting from five to fourteen days was observed in 11 patients who had the cerebral form of malaria. One instance of psychosis was observed in an 8 year old boy who had recovered apparently from severe primary malaria after receiving a total of 1.5 Gm. of quinacrine hydrochloride in seven days of treatment. Twenty-four hours after discharge from the hospital he was readmitted, with a violent maniacal type of psychosis, which responded in five days to treatment with sedatives and parenteral administration of fluids. A 15 month old boy was unable to move his arms and legs or to hold his head up after recovery from the cerebral form of malaria. Improvement was gradual but not complete when bronchopneumonia developed, and the patient died sixty-six days after admission. In a 4 year old girl a flaccid paralysis of the right arm developed after recovery from a primary attack of the cerebral form of malaria. She recovered the complete use of her arm in three months. Severe anemia, with concentrations of hemoglobin below 50 per cent, was observed in 67 patients. Enlargement of the spleen and liver was frequent in children who had had repeated attacks of malaria. There was considerable decrease in the size of these organs at the termination of antimalarial therapy.

The most frequent associated unrelated condition encountered with malaria was intestinal helminthiasis. Two children had bacillary dysentery. Acute exanthemas occurred in 3 children. Tuberculin tests were made on 304 of the 493 patients, and positive reactions were obtained in 47. Although there were only 22 white children in the entire group,

8 of them had positive reactions to tuberculin tests. There was no roentgenologic evidence of pulmonary tuberculosis in any of the patients who gave positive reactions.

PROGNOSIS OF P. FALCIPARUM MALARIA

Twelve, or 2.4 per cent, of the 493 patients with P. falciparum malaria died. These 12 patients were classified as follows: 5 had primary malaria; 4 had questionable primary malaria; 2 had recurrent malaria and 1 had questionable recurrent malaria. Six were boys, and 6 were girls. Eight were mestizo children, 3 were Negroes and 1 was a white child. Their ages ranged from 6 weeks to 12 years. Four deaths occurred in infants 1 year old or younger, six occurred in children between 1 and 6 years and two occurred in children between 7 and 12 years. Eight patients died within twenty-four hours after admission to the hospital. Acute glomerulonephritis in 1 child and a serious congenital heart lesion in another may have been contributory causes of death. Bronchopneumonia, which developed after the malarial infections were well under control, was the cause of death of 2 patients. If these 2 patients are deducted from the 12 who died, then the mortality rate was only 2 per cent instead of 2.4 per cent. Five patients had severe secondary anemia, with concentrations of hemoglobin ranging from 30 to 45 per cent and erythrocytes from 1,500,000 to 2,300,000. Two patients were stuporous and 3 were comatose when admitted to the hospital; 2 others became comatose after admission, and 5 had muscular twitchings, generalized convulsions or both. Autopsies were performed on 10 patients. Malarial pigment or parasites were demonstrated in the brains of 3 and in other internal organs of 6 patients. In the following paragraphs is presented a brief summary of the pertinent data pertaining to each patient who died. A detailed report of the pathologic findings will be published in another report.

Case 1.—A 5 year old white boy was admitted to the hospital with the complaints of fever, abdominal pain, vomiting and diarrhea of two days' duration. There was no history of previous attack of malaria. Residence was in a sanitated community in the Canal Zone. The patient was fairly well nourished and weighed 37 pounds (16.8 Kg.). He was in deep coma. His temperature was 106.2 F.; his pulse was imperceptible, and his respiration was deep and intermittent. The pupils were equal and regular but did not respond to light; there were numerous rhonchi and coarse rales in both lungs, and the spleen was palpable 1 cm. below the left costal margin. The hemoglobin concentration was 55 per cent (Tallqvist); there were 2,600,000 erythrocytes and 12,400 leukocytes. The patient was given one intramuscular injection of 0.1 Gm. of quinacrine hydrochloride but he died two hours after his admission to the hospital.

Anatomic Diagnoses.—The following diagnoses were made: (1) P. falciparum malaria, (2) malarial pigment in the brain, the liver, the spleen and the intestines, (3) edema of the brain and the lungs and (4) splenomegaly.

CASE 2.—A 15 month old mestizo girl was admitted with a history of cough, vomiting, fever and twitching of the muscles of the extremities of three days' duration. There was no history of a previous attack of malaria. Residence was in a sanitated city in the Republic of Panama. She was fairly well nourished and weighed 19 pounds (8,618 Gm.). The child was comatose. Her temperature was 102 F.; her pulse was weak and rapid; the liver and spleen were not palpable. The hemoglobin concentration was 60 per cent; there were 3,100,000 erythrocytes and 9,400 leukocytes. She was given two intramuscular injections of 0.1 Gm. of quinacrine hydrochloride at intervals of four hours. A large dose of barbiturate was administered for sedation. The temperature ranged from 102 to 107 F.; the child had generalized convulsions at intervals of ten to fifteen minutes and died in status epilepticus five hours after her admission to the hospital.

An autopsy was not performed.

CASE 3.—A 12 year old Negro girl was admitted with the complaints of fever, headache, anorexia and vomiting of one day's duration. There was no history of previous attack of malaria. Residence was in a sanitated community in the Canal Zone. The patient walked into the hospital. She was well nourished; her weight was 72 pounds (32.7 Kg.); the temperature was 102.6F.; the liver and the spleen were not palpable. The hemoglobin concentration was 70 per cent; there were 4,000,000 erythrocytes and 7,600 leukocytes. The urine contained albumin (1 plus).

Quinacrine hydrochloride, 0.2 Gm., was administered orally at intervals of six hours. The first two doses were retained. Several hours after the second dose was administered the child began to vomit. Peroral administration was discontinued, and the patient was given only intramuscular injections of the drug in doses of 0.1 Gm. She had two severe generalized convulsions. After these convulsions she became wildly delirious and continued so for about thirty-six hours, when the temperature rose to 107.4 F. and coma supervened. She died fifty-four hours after her admission to the hospital.

Anatomic Diagnoses.—The following diagnoses were made: (1) P. falciparum malaria, (2) congestion of the brain, the lungs and the spleen, (3) fatty metamorphosis of the liver, (4) hepatitis, (5) parenchymatous degeneration of the kidneys and (6) mild atherosclerosis of the aorta.

CASE 4.—A 6 week old mestizo infant was admitted with a history of fever and diarrhea of eight to ten days' duration. He had lived in an unsanitated area since birth. He was well nourished; his weight was 8.5 pounds (3,855 Gm.) and his temperature was 101 F. Moderate pallor was present; the spleen was firm and palpable 2 cm. below the left costal margin. The hemoglobin concentration was 45 per cent; there were 2,000,000 erythrocytes and 8,000 leukocytes. Treatment consisted of the administration of 0.05 Gm. of quinacrine hydrochloride twice daily for seven days and one transfusion of 75 cc. of citrated blood. The malarial infection was well controlled on the seventh day, when acute rhinopharyngitis developed. On the ninth day bronchopneumonia developed, and death occurred three days later.

Anatomic Diagnoses.—The following diagnoses were made: (1) congestion of the leptomeninges, (2) bilateral bronchopneumonia, (3) malarial pigmentation of the spleen and the liver, (4) splenomegaly, (5) focal necrosis of the lymphoid follicles of the spleen, (6) fatty metamorphosis of the liver and (7) congestion and edema of the adrenal glands.

CASE 5.—A 1 year old mestizo girl was admitted with a history of fever, anorexia, vomiting and pallor of four days' duration. There was no history of a previous attack of malaria. Residence was in a sanitated city in the Republic of Panama. She was poorly nourished and weighed 13 pounds (5,896 Gm.). Her tem-

perature was 104 F.; moderate pallor was present; the liver and spleen were not palpable. The hemoglobin concentration was 30 per cent; there were 1,500,000 erythrocytes and 9,500 leukocytes. Quinacrine hydrochloride was administered intramuscularly in doses of 0.05 Gm. at intervals of six hours. The temperature ranged from 96 to 104 F. The child was restless, vomited frequently and died suddenly sixteen hours after her admission to the hospital.

Anatomic Diagnoses.—The following diagnoses were made: (1) cerebral malaria, (2) cerebral edema and congestion, (3) P. falciparum in the liver and the spleen, (4) malarial pigment in the lungs and (5) secondary anemia.

CASE 6.—A 1 year old mestizo boy was admitted with a history of anorexia and fever of four days' duration. There was no history of a previous attack of malaria, although the patient had lived in an unsanitated area since birth. He was poorly nourished, and his weight was 12 pounds (5,443 Gm.). He was moderately dehydrated and apparently comatose. His temperature was 106.2 F.; his pulse was rapid and weak; the liver and the spleen were not palpable. The hemoglobin concentration was 45 per cent; there were 2,300,000 erythrocytes and 12,000 leukocytes. The urine contained albumin (2 plus) and an occasional granular cast. Two doses of 0.1 Gm. of quinacrine hydrochloride were administered intramuscularly at intervals of six hours. The temperature ranged from 102 to 106.2 F., and the patient died nine hours after his admission to the hospital.

Anatomic Diagnoses.—The following diagnoses were made: (1) P. falciparum malaria, (2) congenital heart disease (interventricular septal defect and tricuspid insufficiency), (3) hypertrophy and dilatation of the heart, (4) pericardial effusion, (5) fatty metamorphosis of the liver, (6) edema of the brain, (7) congestion of the meninges, brain, lungs, liver, spleen and kidneys and (8) infection with A. lumbricoides.

CASE 7.—A mestizo girl aged 8 years was admitted with the complaints of fever, vomiting, cough, headache and diarrhea of three days' duration. There was no history of previous attack of malaria although the patient had lived in an unsanitated area since birth. She was in a stupor. She was poorly nourished and weighed 40 pounds (18 Kg.). Her skin was cold and clammy; the temperature was 100.4 F.; the pulse was rapid and weak; the liver and the spleen were not palpable. The hemoglobin concentration was 70 per cent; there were 3,900,000 erythrocytes and 15,200 leukocytes. The urine gave a 1 plus reaction for albumin. The patient was given intramusclar injections of 0.2 Gm. of quinacrine hydrochloride at intervals of six hours and two intravenous injections of isotonic solution of three chlorides. She vomited repeatedly and became comatose when the temperature rose to 106.8 F. Death occurred twelve hours after her admission to the hospital.

Anatomic Diagnoses.—The following diagnoses were made: (1) P. falciparum malaria, (2) congestion and edema of the brain, (3) congestion of the spleen, (4) parenchymatous degeneration of the kidneys and (5) infection with A. lumbricoides, N. americanus and T. trichiura.

CASE 8.—A 5 year old Negro girl was admitted with the complaints of fever and severe diarrhea of two days' duration. There was no history of a previous attack of malaria, although the patient had lived in an unsanitated area since birth. She was fairly well nourished, and her weight was 37 pounds (16.8 Kg.). She was comatose; her temperature was 104.4 F.; the pulse was weak and rapid; the skin was cold and clammy; almost continuous twitchings of the muscles of the face and extremities were present; the liver and the spleen were not palpable. The hemoglobin concentration was 60 per cent; there were 3,200,000 erythrocytes and 11,700 leukocytes. The patient was given two intramuscular injections of 0.1 Gm. of

quinacrine hydrochloride at intervals of four hours. The temperature ranged from 103.8 to 104.4 F.; the pulse became imperceptible, and death occurred five hours after her admission to the hospital.

Anatomic Diagnoses.—The following diagnoses were made: (1) P. falciparum malaria, (2) cerebral edema and congestion, (3) congestion of the lungs, the kidneys and the spleen, (4) focal necrosis of the liver and (5) parenchymatous degeneration of the kidneys.

CASE 9.—An 8 month old Negro girl was admitted to the hospital with a history of fever and diarrhea of four days' duration. There was no history of a previous attack of malaria, although the patient had lived in an unsanitated area since birth. She weighed 16.5 pounds (7,484 Gm.). Dyspnea, pallor and dehydration were pronounced. The spleen was barely palpable. The temperature ranged from 100.2 to 100.8 F. The hemoglobin concentration was 35 per cent; there were 1,500,000 erythrocytes and 7,400 leukocytes. Lactate Ringer solution was administered subcutaneously, and, because of vomiting, quinacrine hydrochloride, in doses of 0.05 Gm., was administered intramuscularly at intervals of six hours. The child died twelve hours after her admission to the hospital, just before she was to receive a transfusion of blood.

Anatomic Diagnoses.—The following diagnoses were made: (1) P. falciparum malaria, (2) malarial pigmentation of the liver and the spleen and (3) secondary anemia.

CASE 10.—A 15 month old mestizo boy was admitted with a history of fever, anorexia, diarrhea, rapid breathing and convulsions of one day's duration. The patient had been in another hospital for P. falciparum malaria four weeks previously. He had lived in an unsanitated area since birth. He appeared to be in a stupor. He was poorly nourished, weighing only 17 pounds (7,711 Gm.); his temperature was 104 F.; his pulse was rapid and weak; slight twitchings of the muscles of the extremities were present; the spleen was firm in consistency and palpable 3 cm. below the left costal margin. The hemoglobin concentration was 45 per cent; there were 2,200,000 erythrocytes and 10,200 leukocytes. Three doses of 0.1 Gm. of quinacrine hydrochloride were administered intramuscularly at intervals of six hours and then orally in doses of 0.1 Gm. twice daily for six days. Fluids were given subcutaneously as required, and one blood transfusion was administered. Several generalized convulsions occurred on the first day. The temperature ranged from 100 to 105.2 F. for three days and then returned to normal. On the fifth day it was observed that the patient had a blank facial expression; he rolled his head from side to side; he was unable to move his arms or legs or hold his head up without support. The cerebrospinal fluid was normal, and repeated blood smears were negative for P. falciparum. Improvement was gradual but not complete when, two months after admission, acute suppurative otitis media and bronchopneumonia developed. Death occurred sixty-six days after admission of the patient to the hospital.

An autopsy was not performed.

CASE 11.—A mestizo boy aged 6 years was admitted with complaints of chills and fever, vomiting and headache of two days' duration. The patient had been hospitalized in another hospital for P. falciparum malaria three months previously. He had lived in an unsanitated area since birth. The patient was in a deep coma; he was well nourished; his weight was 45 pounds (20.4 Kg.); his temperature was 101.4 F.; his pulse was weak and rapid; almost continuous twitchings of the muscles of the extremities were present; the liver and the spleen were not palpable. The hemoglobin concentration was 65 per cent; there were 3,400,000 erythrocytes

and 9,100 leukocytes. Quinacrine hydrochloride, in doses of 0.1 Gm., was administered intramuscularly at intervals of six hours. The temperature rose to 104.4 F., and death occurred seven hours after the patient was admitted to the hospital.

Anatomic Diagnoses.—The following diagnoses were made: (1) P. falciparum malaria, (2) malarial parasites and pigment in the brain, the spleen, the bone marrow and the blood, (3) congestion of the brain, with numerous intraparenchymal hemorrhages, (4) congestion of the leptomeninges, with small subarachnoid hemorrhages, (5) congestion of the spleen and (6) infection with N. americanus and T. trichiuris.

CASE 12.—A mestizo boy aged 5 years was admitted with the complaints of chills and fever of seven days' duration and swelling of his face, lower extremities and abdomen of four days' duration. Although there was no history of a previous attack of malaria, the patient had had frequent bouts of fever of undetermined origin and had lived in an unsanitated area since birth. He was well nourished and weighed 40 pounds (18.1 Kg.); his temperature was 102 F.; his pulse was rapid and full. The blood pressure was recorded as 132 systolic and 90 diastolic. Moderate generalized edema was present; the abdomen was distended; the spleen was firm and palpable 2 cm. below the left costal margin. The hemoglobin concentration was 55 per cent; there were 3,100,000 erythrocytes and 6,400 leukocytes. The urine contained albumin (4 plus), numerous erythrocytes and granular casts. Quinacrine hydrochloride, in doses of 0.1 Gm., was administered intramuscularly at intervals of six hours for two doses and then orally twice daily. The patient was given one injection of 10 cc. of 25 per cent solution of magnesium sulfate. The temperature ranged from 98.2 to 104 F.; oliguria was pronounced, and death occurred forty hours after his admission to the hospital.

Anatomic Diagnoses.—The conditions observed were diagnosed as (1) pulmonary edema, (2) bilateral pleural effusion, (3) bronchopneumonia in the lower lobes of both lungs, (4) pericardial effusion, (5) tigroid markings of the endocardium, (6) acute parenchymatous degeneration of the myocardium, (7) peritoneal effusion, (8) splenomegaly, (9) acute toxic splenitis, (10) malarial parasites and pigment in the spleen, the bone marrow and the liver, (11) congestion of the adrenal glands, (12) congestion of the small intestine, (13) infection with A. lumbricoides and N. americanus, (14) acute glomerulonephritis and (15) secondary anemia.

TREATMENT

The drugs used in the treatment of P. falciparum malaria were quinacrine hydrochloride, quinine and pamaquine naphthoate. Although these drugs are regarded as specific agents in the treatment of malaria, the fact remains that this disease is difficult to cure completely. This was evident from the number of patients who, after having received adequate therapy for a primary attack, suffered relapses even though they had had no apparent opportunity of becoming reinfected. There were 9 children who lived where the opportunity for reinfection was negligible but who had periods of renewed activity even after adequate treatment.

Treatment with Quinine.—Quinine was administered to 108 patients (table 9). The preparations used were quinine sulfate for oral administration and quinine dihydrochloride for intravenous or intramuscular

TABLE 9.—*Drugs Employed in the Treatment of P. Falciparum Malaria*

Drug	Type of Malaria				
	Primary	Questionable Primary	Recurrent	Questionable Recurrent	Total Number of Cases
Quinacrine hydrochloride	101	40	83	80	304
Quinine	31	5	14	40	90
Quinacrine hydrochloride and quinine	4	2	2	4	12
Quinacrine hydrochloride and pamaquine naphthoate	25	7	17	13	62
Quinine and pamaquine naphthoate	4	5	0	9	18
Quinacrine hydrochloride, quinine and pamaquine naphthoate	1	0	4	2	7

administration. The following dosages, administered three times daily at regular intervals of four hours, were adopted for use in this series of patients:

Age less than 1 year, ½ grain (0.03 Gm.).
One year, 1 grain (0.06 Gm.).
Two years, 2 grains (0.13 Gm.).
Three and 4 years, 3 grains (0.19 Gm.).
Five and 6 years, 4 grains (0.26 Gm.).
Seven and 8 years, 5 grains (0.32 Gm.).
Nine and 10 years, 6 grains (0.39 Gm.).
Eleven and 12 years, 7 grains (0.45 Gm.).

The drug was discontinued after one week, and none was administered after the patient's discharge from the hospital. The drug was usually administered orally; infants and younger children received it dissolved in a solution of sulfuric acid, and older children received it in the form of tablets. Quinine dihydrochloride was administered intravenously to 7 patients and intramuscularly to 5. A sterile abscess formed in 1 patient following intramuscular administration. Trophozoites disappeared from the peripheral blood in all the patients treated with quinine in from one to four days, with an average of two days. In 4, or 3.7 per cent, gametocytes developed after one week of therapy. In chart 2 may be seen the average temperature curve of all the quinine-treated patients with primary and recurrent P. falciparum malaria. This average temperature curve has been contrasted with similar curves established for the patients treated with quinacrine hydrochloride. No important differences between the response of fever to quinine or quinacrine hydrochloride in primary or recurrent P. falciparum malaria were

observed. Similar observations were made in the patients with questionable primary and questionable recurrent malaria.

Toxic effects due to quinine, particularly idiosyncrasy, ringing in the ears, deafness, dyspnea, cyanosis and various cutaneous rashes have been reported. These reactions were rarely observed in the children treated with quinine, although older patients occasionally complained of ringing in their ears. Vomiting occurred frequently. Usually this symptom was present on admission to the hospital. Even though it

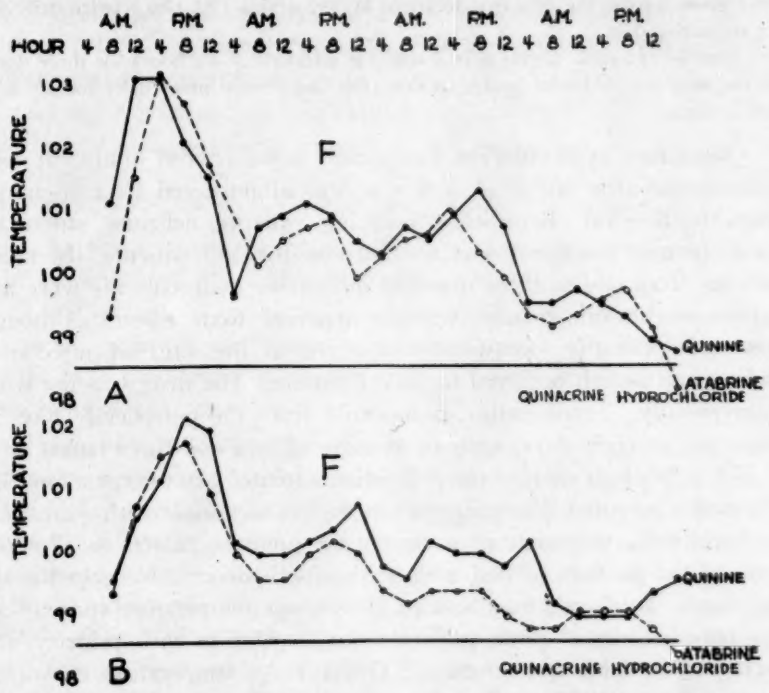

Chart 2.—*A*, response of the temperature in primary P. falciparum malaria to therapy. The solid line represents the average temperature curve of the patients treated with quinine; the broken line represents the average temperature curve of the patients treated with quinacrine hydrochloride. *B*, response of the temperature in recurrent P. falciparum malaria to therapy. The solid line represents the average temperature curve of the patients treated with quinine; the broken line represents the average temperature curve of the patients treated with quinacrine hydrochloride.

continued for a variable period, it could not be stated with finality that vomiting was either caused or aggravated by quinine.

Treatment with Quinacrine Hydrochloride.—Quinacrine dihydrochloride for peroral treatment was available in tablets of ¼ grain (0.05 Gm.) and 1½ grain (0.1 Gm.). For intramuscular administration ampules containing 3 grains (0.2 Gm.) of sterile powder accompanied with 10 cc. ampules of distilled water were available. This drug was used

for 385 patients (table 9). The following dosages were adopted for use in this series of patients:

Age less than 1 year: ¾ grain (0.05 Gm.) at intervals of eight hours for two doses during the first day, followed by ¾ grain (0.05 Gm.) once daily for six successive days.

One to 4 years inclusive: ¾ grain (0.05 Gm.) at intervals of six hours for three doses during the first day, followed by ¾ grain (0.05 Gm.) twice daily for six successive days.

Five to 8 years inclusive: 1½ grains (0.1 Gm.) at intervals of six hours for three doses during the first day, followed by 1½ grains (0.1 Gm.) twice daily for six successive days.

Nine to 12 years: 3 grains (0.2 Gm.) at intervals of six hours for three doses on the first day, followed by 1½ grains (0.1 Gm.) three times daily for six successive days.

Quinacrine hydrochloride was usually administered orally. It was discontinued after one week, and none was administered after discharge from the hospital. Because of vomiting, collapse, delirium, stupor or coma, peroral treatment was not feasible for 143 patients. In these patients from one to three doses of quinacrine hydrochloride were administered intramuscularly, without apparent toxic effect. Although areas of induration occasionally occurred at the sites of injections, abscess and slough occurred in only 1 patient. The drug was not used intravenously. Trophozoites disappeared from the peripheral blood in from one to eight days, with an average of two and three-tenths days in 373, or 96.9 per cent, of the 385 patients treated. In the remaining 12, Plasmodia persisted throughout seven days of treatment with quinacrine hydrochloride, necessitating a change to quinine. In 69, or 17.9 per cent, of the patients treated with quinacrine hydrochloride gametocytes developed. In chart 2 may be seen the average temperature curve of all the patients treated with quinacrine hydrochloride with primary and recurrent P. falciparum malaria. This average temperature curve has been contrasted with similar curves established for the quinine-treated patients. No important differences between the response of fever to quinacrine hydrochloride or quinine were observed.

Toxic effects due to quinacrine hydrochloride, particularly headache, prostration, rashes and vomiting, have been reported. These reactions were rarely observed in the children treated with quinacrine hydrochloride. In almost all the patients treated with this drug, a yellow discoloration of the skin and scleras developed on the third to the fifth day of treatment and disappeared in two to four weeks. This was interpreted as being due to a deposition of the drug in the tissues and a harmless rather than a toxic symptom. In no instance was the use of quinacrine hydrochloride discontinued because of this coloration of the skin. Concurrently with coloration of the skin, the urine became yellow due to the presence of the dye. In an 8 year old boy an acute maniacal

type of psychosis developed, which was thought to have been due to quinacrine hydrochloride. Response to treatment with sedatives and fluids administered parenterally was prompt and without apparent residual effects.

Pamaquine Naphthoate.—Pamaquine naphthoate was available in tablets of 1/6 grain (0.01 Gm.). It was administered to the 73 patients who had gametocytes in the peripheral blood after treatment with quinine or quinacrine hydrochloride (table 9). It was not used alone in the treatment of the acute attacks of P. falciparum malaria. The following dosage was usually given on five successive days or until the gametocytes disappeared:

Age less than 1 year, 1/12 grain (0.005 Gm.) once daily.
One to 4 years inclusive, 1/6 grain (0.01 Gm.) once daily.
Five to 8 years inclusive, 1/6 grain (0.01 Gm.) twice daily.
Nine to 12 years inclusive, 1/6 grain (0.01 Gm.) three times daily.

Gametocytes persisted for from three to twelve days after therapy with pamaquine naphthoate was instituted.

Toxic effects from pamaquine naphthoate, particularly cyanosis, dizziness, epigastric discomfort, headache, nausea and methemoglobinemia, have been reported. These effects were not observed in the children treated with this drug.

General Treatment.—Patients were confined to bed as long as acute symptoms were present. The administration of fluids was urged during the febrile stage. When vomiting, diarrhea and dehydration were present, fluids were administered parenterally as indicated. The intravenous administration of 5 per cent dextrose in isotonic solution of three chlorides early and frequently in the treatment of the algid and cerebral forms of malaria seemed to be of paramount importance. Hydrotherapy was useful in the combating of hyperpyrexia. Large doses of barbiturates were administered to the patients with cerebral malaria and convulsions. As soon as recovery from the acute symptoms occurred, appropriate anthelminthic drugs were administered to those who had intestinal helminthiasis. The administration of iron was of value in the treatment of secondary anemia. The response to hematinics after the malarial infections were controlled and the burdens of worms reduced were excellent in most cases. In 11 children with severe anemia, one or more transfusions of blood were necessary. Amyl nitrite as an inhalant or intravenous injections of epinephrine for the purpose of making the parasites more accessible to quinine were not used in this series of patients.

COMMENT

An analysis of the ages of the children treated for P. falciparum malaria in hospitals in the Canal Zone showed that these children could

have and did acquire their first infections shortly after birth. Clark [13] demonstrated that many children living in unsanitated endemic districts in the Canal Zone and adjoining areas harbor malarial parasites in their blood without showing serious symptoms of the disease. However, the adults living in the same areas have lower rates of infection. This would indicate that some degree of acquired immunity may result from repeated and persistent infection in early life. The character and location of the immune response are questions of considerable controversy. Boyd, Stratman-Thomas and Kitchen [14] demonstrated that reinoculation of a patient with the same strain of P. falciparum from which he had recovered did not result in a second attack, although Plasmodia were demonstrable in the peripheral blood for as long as four months. However, an attack of malaria resulted when such a patient was reinoculated with a different strain of the same species of Plasmodium. By showing that recent recovery from infections with either P. vivax or P. falciparum was no obstacle to successful reinoculation with other species of the parasite, they demonstrated the absence of a cross immunity between these two infections. In their studies of extracellular immunity in Plasmodium knowlesi malaria in rhesus monkeys, Eaton and Coggeshall [15] demonstrated the existence of specific protective antibodies in the serum during the stage of chronic infection. The concentration of these antibodies varied during the course of the disease, being decreased preceding a relapse and increased at the termination of the relapse. They also demonstrated the existence of complement-fixing and agglutinating antibodies in the serums of monkeys with chronic malarial infections. These observations seem to point to the existence of extracellular immunity in malaria in rhesus monkeys.

The data indicating that in 75, or 15.2 per cent, of the patients P. falciparum malaria developed in sanitated areas are misleading. Human beings wander about considerably. Most of them cannot honestly recall where they have been every waking hour of the day or night over a period corresponding to the incubation period of malaria. Actually a miracle has been accomplished by sanitation on the Isthmus of Panama. When a history indicating that a child has acquired malaria in a sanitated area is obtained, such information must be interpreted in the light of such knowledge of the activities of human beings.

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13. Clark and Komp.[11] Clark.[12]

14. Boyd, M. F.; Stratman-Thomas, W. H., and Kitchen, S. F.: On Efficiency of Homologous Properties of Acquired Immunity to Plasmodium Vivax, Am. J. Trop. Med. **16**:447-457 (July) 1936; On Acquired Immunity to Plasmodium Falciparum, ibid. **16**:139-145 (March) 1936.

15. Eaton, M. D., and Coggeshall, L. T.: Production in Monkeys of Complement-Fixing Antibodies Without Active Immunity by Injection of Killed Plasmodium Knowlesi, J. Exper. Med. **70**:141-146 (Aug.) 1939.

Toxic reactions from either quinine or quinacrine hydrochloride were uncommon. From the point of view of toxicity, the selection of one drug in preference to the other offers nothing of value. In so far as the effect on fever is concerned, quinacrine hydrochloride seems to produce the same result as quinine. Reference to chart 2 indicates clearly that the return of temperature to normal occurred as quickly in the patients treated with quinacrine hydrochloride as it did in the patients treated with quinine. Either drug, if started during or shortly after the first paroxysm in a child, will usually diminish the severity of the second and prevent completely the occurrence of the third. Trophozoites disappeared from the peripheral blood in the quinine-treated patients in an average of two days, as compared with two and three-tenths days in those treated with quinacrine hydrochloride. In these patients again there was no striking evidence that the response of P. falciparum malaria to quinacrine hydrochloride was materially slower than the response to quinine. Quinacrine hydrochloride had little or no effect against the gametocytes of P. falciparum, although these sexual forms were observed in patients treated with quinine as well as in those treated with quinacrine hydrochloride. In all probability quinine does not destroy gametocytes, but it does destroy the schizonts, from which the gametocytes develop. It has been thought that fewer relapses occur after treatment with quinacrine hydrochloride than after therapy with quinine. This difference, however, was not apparent in the present study. Bercovitz [16] felt that quinine and not quinacrine hydrochloride should be used in the treatment of malaria in children under 5 years. Both Manson-Bahr [17] and Hasselman [18] stated that the treatment of severe P. falciparum malaria should begin with administration of quinine and that if quinacrine hydrochloride is used a few doses of quinine should be given along with it. This practice was followed in several of the earlier desperately ill patients probably because of timidity or lack of confidence in the efficacy of quinacrine hydrochloride on the part of attending physicians. More recently, however, the efficacy of quinacrine hydrochloride in the treatment of severe (pernicious) P. falciparum malaria in children has been more thoroughly appreciated. Now quinacrine hydrochloride is the sheet anchor in the treatment of such patients. It has been learned that the cerebral and algid forms of P. falciparum malaria in children are medical emergencies and require the constant vigilance of the attending

16. Bercovitz, Z. T.: Clinical Tropical Medicine, ed. 1, New York, Paul B. Hoeber, Inc., 1944, p. 181.

17. Manson-Bahr, P. H.: Manson's Tropical Diseases, ed. 11, Baltimore, William Wood & Company, 1940, p. 119.

18. Hasselman, C. M.: Zum Mechanismus der Nebenwirkungen des Plasmochins und über dessen therapeutische Wirkungsgrenzen bei autochthoner Malaria in den Tropen, Arch. f. Schiffs- u. Tropen-Hyg. **44**:275-281 (June) 1940.

physician. An early diagnosis, the early intramuscular administration of quinacrine hydrochloride and the early and frequent administration of fluids subcutaneously or intravenously have given results comparable to those obtained with quinine.

The dosage of quinacrine hydrochloride recommended for children and followed in the hospitals in the Canal Zone with slight modification needs careful examination. If the average weights for boys as given by Griffith and Mitchell[9] are accepted as standards, the following dosages are found to prevail:

Age, Years	Average Weight, Pounds	Total Amount of Drug, Gm.
1	21 (9.5 Kg.)	0.75
4	37 (16.8 Kg.)	0.75
5	41 (18.6 Kg.)	1.50
8	53 (24 Kg.)	1.50
9	59 (26.8 Kg.)	2.40
12	75 (34 Kg.)	2.40

Thus a 1 year old boy and a 4 year old boy receive exactly the same amount of drug even though one weighs almost twice as much as the other. Comparable inconsistencies exist in the other age groups. Thus with the variations in weight at different age levels a poorly nourished 1 year old child weighing 18 pounds (8.2 Kg.) or less will receive the same amount of drug as a well nourished child of 4 years weighing 40 pounds (18.1 Kg.) or more. Adjustments are made in the hospitals in the Canal Zone so that larger children receive larger amounts of the drug than is recommended for their chronologic age and vice versa. Such a method is arbitrary and subject to criticism just as is the method of fixed dosage. It seems much more reasonable to base the dosage of quinacrine hydrochloride on the actual weight of the child. Reference to the figures listed reveals that the total number of grams of quinacrine hydrochloride received by the smallest child in each group is approximately 1/30 of the body weight in pounds. If one uses this figure, an infant weighing 16 pounds (7.3 Kg.) would receive a total of 0.53 Gm. and a child weighing 48 pounds (21.8 Kg.) would receive 1.6 Gm. of the drug. To determine the amount of drug to be administered daily, the total number of grams of quinacrine hydrochloride is divided by 8. On the first day, twice the daily dose is administered at intervals of six hours. During the next six days three doses are given daily, each dose being one third of the total daily dose, e.g.,

1. Given a child weighing 60 pounds.
2. Total amount of drug $\frac{\text{Weight of child (60 lbs.)}}{8}$ equals 2.0 Gm.
3. Total daily dosage $\frac{2 \text{ Gm.}}{8}$ equals 0.25 Gm.

4. Total dosage first day 0.25 Gm. times 2 equals 0.5 Gm., or 0.17 Gm. at intervals of six hours for three successive doses.

5. Dosage from second to seventh days inclusive $\frac{0.25 \text{ Gm.}}{3}$ equals 0.08 Gm. daily at intervals of four hours.

Of 2 children each weighing 48 pounds, one of whom is 6 years old and overweight and the other 10 years old and underweight, each would receive exactly the same amount of quinacrine hydrochloride. By the method in use at the present time, the younger child would receive 1.5 Gm. and the older child would receive 2.4 Gm. of the drug. Smaller tablets, containing ¼ grain (0.017 Gm.), of quinacrine hydrochloride should be made available for the treatment of malaria in children.

Much has been done in the Canal Zone and some adjacent regions in the Republic of Panama in the prevention of malaria. These measures have been directed at (1) the destruction of anopheline mosquitoes and their breeding places and (2) the protection of persons from the bites of mosquitoes. The use of drug prophylaxis among the natives has been found to be impractical. More important has been the continuous search for and treatment of carriers in endemic regions. The drug of choice in this area as in others has been quinacrine hydrochloride.

SUMMARY

In the Canal Zone and adjoining areas of the Republic of Panama, the malarial fevers occupy a position of clinical significance in pediatric practice second only to intestinal helminthiasis.

Estivoautumnal, or P. falciparum, malaria is commoner than tertian, or P. vivax, malaria, the ratio being 1.48:1.

Breeding of the anopheline vectors of P. falciparum malaria continues throughout the year.

P. falciparum malaria is observed throughout the year. The number of cases varies from month to month and from year to year, although peaks occur during the change of seasons.

The incidence of P. falciparum malaria is definitely related to the degree of development of sanitation. Although 15.2 per cent of the patients live in completely sanitated United States government communities and principal cities of the Republic of Panama, 84.8 per cent live in unsanitated rural or semirural communities. Infection is much commoner among mestizo children, who for the most part live in unsanitated districts, than it is among white children, who almost exclusively live in sanitated communities.

Infection with P. falciparum may occur any time after birth. Approximately one fifth of the children in Panama have had at least one attack of malaria by the end of their second year of life.

In 41.3 per cent of the patients, P. falciparum malaria occurs in association with other conditions, the commonest of which is intestinal helminthiasis.

The paroxysm of P. falciparum malaria in children does not follow the typical pattern observed in adults. The following important differences are observed: (1) Prodromal symptoms are frequent; (2) the cold, hot and sweating stages are indistinct; (3) a chill does not occur in one half of the patients and seems to be replaced by such symptoms as vomiting and convulsions; (4) the temperature is irregular or more or less continuous; (5) delirium, stupor, coma, muscular twitchings and convulsions are common.

The terms cerebral, gastralgic, algid, bilious, remittent and hemorrhagic are used to describe the severe character of the symptoms which occur in some cases of P. falciparum malaria. They do not refer to particular disease entities.

Abnormal physical signs were uncommon in primary P. falciparum malaria. Splenomegaly, hepatomegaly, pallor and underweight were frequently observed in patients with recurrent malaria.

The differential diagnosis of P. falciparum in thick and thin blood smears depends on recognition of the features characteristic of infection with that species of parasite.

The absence of parasites in the peripheral blood as determined by three successive smears negative for malarial organisms obtained daily over a period of three days does not mean that the malarial infection has been eradicated. Patients generally return to their homes in unsanitated areas. In such circumstances the final differentiation between reinfection and relapse cannot be made.

During periods of renewed activity, the latent P. falciparum malaria observed in children living in unsanitated areas resembles the malaria observed in children treated in hospitals.

The mortality rate is 2 per cent. Eighty per cent of the deaths occur within twenty-four hours after admission to the hospital.

Neither quinacrine hydrochloride (atabrine) nor quinine is effective against the gametocytes of P. falciparum. The disappearance of trophozoites from the peripheral blood in patients treated with quinacrine hydrochloride is slightly slower than that in patients treated with quinine. Quinine offers no material advantages over quinacrine hydrochloride insofar as toxicity, effect on fever and the number of paroxysms after institution of therapy are concerned.

The pernicious forms of P. falciparum malaria in children are medical emergencies. Successful management of these patients depends on the following: (1) an early diagnosis; (2) a high blood level of quinacrine hydrochloride attained quickly by intramuscular administration of this drug and (3) early and frequent administration of fluids subcutaneously or intravenously.

The dosage of quinacrine hydrochloride should be based on the weight rather than on the chronologic age of a child.

CLINICAL ASCARIASIS

An Analysis of Two Hundred and Two Cases

J. CLYDE SWARTZWELDER, Ph.D
NEW ORLEANS

STUDIES by Faust,[1] Headlee[2] and Moss[3] on the incidence of intestinal parasites in and around New Orleans have demonstrated the relatively common occurrence of ascariasis in this area. Also, of 11,000 stools of clinic and hospitalized patients at the Charity Hospital in this city examined by my associates and me, 426 were found to contain ova of Ascaris lumbricoides.

In view of the common occurrence of ascariasis in this metropolitan area and of my opportunity to observe numerous cases of this helminth infection, I am presenting an analysis of the clinical and laboratory data from the case records of 202 patients with clinically evident A. lumbricoides infection admitted to the Charity Hospital of Louisiana during a period of about a decade.

The cases in this series met the following criteria:

1. Only patients with clinically evident infection who were hospitalized and for whom a satisfactory history and physical examination were obtained have been included.

2. Either the ova of A. lumbricoides or the adult worms or both were demonstrated.

3. The parasitic infection was of primary significance and apparently not secondary to some other disease. Patients with ascariasis who harbored other pathogenic parasites, with the exception of a few persons who had light infections with Trichuris trichiura, were not included.

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1. (*a*) Faust, E. C.: Parasitic Infections in New Orleans Based on a Cross Section of Charity and Welfare Clinic Patients with Especial Reference to the Children's Clinic, J. Pediat. **2**:53-58 (Jan.) 1933. (*b*) Faust, E. C., and Headlee, W. H.: Intestinal Parasite Infections of the Ambulatory White Clinic Population of New Orleans, Am. J. Trop. Med. **16**:25-28 (Jan.) 1936.

2. Headlee, W. H.: The Epidemiology of Human Ascariasis in the Metropolitan Area of New Orleans, Louisiana, Am. J. Hyg. **24**:479-521 (Nov.) 1936. Faust and Headlee.[1b]

3. Moss, E. S.: The Incidence of Intestinal Parasites: An Analysis of 2,265 Routine, Consecutive Stool Examinations in the Out-Patient Dispensaries of Charity Hospital of Louisiana at New Orleans, Am. J. Clin. Path. **9**:437-447 (July) 1939.

4. A careful study of the case history indicated that the complaint which brought the patient to the hospital could justifiably and reasonably be attributed to the parasitic infection. The diagnosis on discharge in all cases was either ascariasis or intestinal obstruction due to A. lumbricoides. These criteria excluded asymptomatic ascaris infections, cases of mild infection such as are treated in the clinics and those infections with Ascarides which were of secondary importance to other diseases or complicated by other diseases or parasitic infections.

ANALYSIS OF DATA

Age, Race and Sex.—In this series of cases the age ranged from less than 1 year to 48 years. One hundred and seventy of the 202 patients were under 16 years of age. The maximum number of cases per year of age, 33 cases, were those of children 2 years of age. Seventy-six cases were of children 5 years of age or under. Faust and Headlee [1b] found that A. lumbricoides had the highest incidence of any helminth in this age group among white patients of clinics in New Orleans and considered that both epidemiologically and clinically it was probably the

TABLE 1.—*Distribution By Age*

Age, Years	Number of Patients
1 - 5	76
6 - 10	57
11 - 15	37
16 - 20	12
21 - 30	5
Over 30	15
Total	202

most important parasite of this age group. That clinical ascariasis is not limited to children is indicated by the fact that 15 patients were over 30 years of age. Thus, although the infection is more commonly found in children, it must also be considered clinically in adults.

The Negro patients represented approximately 30 per cent of the entire group of patients studied. Since there was only a slight difference between the percentages of white and of Negro patients admitted to the hospital in the same period, some other factor is necessary to explain the preponderance of the white patients in this series over the Negro group. According to Headlee,[2] the environments inhabited by Negro families in New Orleans were found to be more heavily infested, on the basis of the number of ascaris eggs isolated from the soil, than were those inhabited by white families. In view of the lower standard of sanitary facilities for the Negro race in this area, the smaller number of clinical cases of the Negro group is contrary to what might be expected. A somewhat

similar, unexplained condition was reported by me [4] for infections with Trichuris trichiura in this area, wherein Negro patients represented less than one sixth of a series of 81 patients with clinically evident trichuriasis.

The numbers of males and females in the series were approximately equal. Of the persons over fifteen years of age, 19 were females and 13 were males.

TABLE 2.—*Distribution by Sex and Race*

	No. of Patients	Female	Male
White	143	75	68
Negro	59	27	32
Total	202	102	100

Seasonal Incidence.—There was no significant seasonal incidence of cases, as the distribution by monthly admission was fairly uniform. The ability of the eggs of A. lumbricoides to remain viable for long periods and to withstand rigorous environmental conditions, owing to the insulation afforded by their shell layers, probably permits year-round infectivity of the ova of the parasite in this area. In Louisiana, the mild climate through the winter months also affords the opportunity for continued exposure of children whose play habits bring them in close contact with soil which may be "seeded" with Ascaris eggs due to pollution by excreta of infected persons.

TABLE 3.—*Distribution of Patients By Month of Admission*

	No. of Patients		No. of Patients
January	21	July	18
February	12	August	17
March	20	September	16
April	16	October	16
May	20	November	17
June	17	December	12

Symptomatology.—The most common chief complaints at the time of admission, in order of frequency, were: abdominal pain or discomfort, passage of worms, fever, vomiting, convulsions, and cough or cold. Abdominal pain or distress appeared as a chief complaint in 112 cases, or for more than one half of the persons in the series. The subject of abdominal pain will be given more detailed analysis later. The wide

4. Swartzwelder, J. C.: Clinical Trichocephalus Trichiurus Infection: An Analysis of Eighty-One Cases, Am. J. Trop. Med. **19**:473-481 (Sept.) 1939.

variety of chief complaints that were given by a few persons is apparent in table 4.

TABLE 4.—*Chief Complaints*

	No. of Patients		No. of Patients
Abdominal pain or discomfort	112	Pain in chest	3
Passage of worms	35	Backache	3
Fever	34	Vertigo	2
Vomiting	32	Dyspnea	2
Convulsions	19	Malaise	2
Cough or cold	16	Loss of weight	2
Diarrhea	11	Anorexia	1
Constipation	9	Abdominal distention	1
Headache	6	Fainting spells	1
Weakness	6	Jaundice	1
Nausea	5	Hemoptysis	1
Nervousness	4		

The patients were moderately to acutely ill. Six of the cases of intestinal obstruction terminated fatally. The clinical manifestations, including the chief complaints, the other symptoms, and the physical findings, are shown in table 5. The most common symptoms and

TABLE 5.—*Clinical Manifestations (Including Chief Complaints, Other Symptoms and Physical Findings)*

	No. of Patients		No. of Patients
Abdominal pain or discomfort	139	Dyspepsia	9
Passing ascarids (through anus, mouth or nose)	133	Dyspnea	8
Vomiting	77	Alternating constipation and diarrhea	6
Abdominal or epigastric tenderness	71	Vertigo	6
Fever	56	Insomnia	6
Constipation	51	Drowsiness	6
Abdominal distention	50	Grating or grinding of teeth	5
Cough or cold	45	Blood and mucus in stool	4
Nausea	38	Pain in chest	4
Headache	28	Increased appetite	3
Diarrhea	26	Facial edema	3
Convulsions	23	Chills	3
Abnormal pulmonary findings	23	Pain in back	3
Anorexia	16	Hysteria	2
Loss of weight	15	Irritation in throat	2
Weakness	11	Tenseness	2
Malaise	10	Fainting	1
Restlessness	10	Pruritus nasi	1
Abdominal rigidity	9	Pallor	1
Abdominal mass palpated	9	Jaundice	1
		Hemoptysis	1

observations, in order of their frequency, were: abdominal pain or discomfort, passing of ascarids (by mouth, anus or nose), vomiting, abdominal or epigastric tenderness, fever, constipation, abdominal distention, cough or cold, nausea, headache, diarrhea and convulsions. A variety of other clinical manifestations occurred in a lesser number of cases and appear in table 5. Many of these manifestations were probably

attributable to helminth toxemia or to mechanical obstruction of the intestine by the parasites. The physical findings are shown in table 6.

Ninety-four persons gave a history of passing adult ascarids in the stool or passed ascarids after an enema, prior to anthelmintic medication. In 35 cases adult worms were vomited or passed by mouth. One patient passed a total of fourteen adult worms by mouth in one day. Four persons passed worms per nares. Many of the patients harbored a large number of worms. Several hundred adult worms were reportedly found in a fatal case of obstruction. In another case, 85 worms were removed surgically. In a fatal case of obstruction following the use of carbon tetrachloride, adult worms were found at autopsy from the stomach to the colon, and the jejunum was tightly packed with worms.

TABLE 6.—*Physical Observations*

	Number of Patients
Abdominal or epigastric tenderness	71
Abdominal distention	50
Abnormal pulmonary condition (determined by examinations, physical and roentgenologic)	23
Abdominal rigidity	9
Mass in abdomen palpated	9

Some persons volunteered the information that they had been passing worms intermittently for several years.

Respiratory complaints included asthmatic attacks, cough, a history of frequent or chronic colds, pain in the chest, dyspnea and irritation in the throat. The cough was usually nonproductive. The frequent occurrence of respiratory complaints prior to the abdominal complaints is consistent with the pulmonary phase of this infection, which precedes intestinal infection by the adult worms. In 1 case there was a history of chronic bronchitis for seven years, throughout which ascarids were frequently passed in the stool. In 23 cases there was evidence, either from physical or from roentgen examination, of abnormal pulmonary conditions, such as rales or peribronchial infiltration. Owing to difficulty in differentiation, it is possible that in a few of the cases the respiratory complaints and manifestations which were ascribed to ascariasis may have been due to infection of the upper respiratory tract of other causation. However, they were not considered as complications nor included as such in the final diagnosis by the attending physician.

Abdominal pain, the most common symptom and complaint, was frequently sudden in onset and recurrent. It was most commonly located in the region of the epigastrium and umbilicus. The abdominal pain was located in the right lower quadrant of the abdomen or was generalized in a significant number of cases, as shown in table 7.

TABLE 7.—*Location of Abdominal Pain*

	No. of Patients		No. of Patients
Epigastric	24	Right upper quadrant	4
Umbilical	23	Left upper quadrant	4
Right lower quadrant	17	Left lower quadrant	1
Generalized	14	Upper part of abdomen	1
Lower part of abdomen	8	Location not given	33

Temperatures above 101 F. were associated primarily with intestinal obstruction or with signs of helminth toxemia. Respiratory complaints were absent in many of the 33 persons with a temperature above 101 F., and thus could not have accounted for the fever. Sixty-five persons had temperatures between 99.1 and 101 F.

TABLE 8.—*Temperatures*

	No. of Patients		No. of Patients
Less than 99 F.	94	Above 101 F.	33
99.1 to 100 F.	48	Not given	10
100.1 to 101 F.	17		

In 67 cases, or about one third of the series, the symptoms were evident for a week or less prior to admission. In 69 cases the complaints which brought the patients to the hospital had been experienced intermittently for more than three months. In some instances the duration of symptoms was given as several years. Reinfection commonly occurs in ascariasis, and, in addition to persistent infection, could account for continued infection over a long period.

TABLE 9.—*Duration of Symptoms Before Admission*

Duration	No. of Patients	Duration	No. of Patients
1 day	20	7 to 12 months	4
2 days to 1 week	47	1 to 2 years	29
1 week to 1 month	44	3 to 5 years	10
1 to 3 months	22	6 to 10 years	3
4 to 6 months	14	Not given	9

Intestinal Obstruction.—In 18 of the cases the diagnosis was intestinal obstruction, including transitory, partial or complete obstruction. The bases for the diagnosis of intestinal obstruction were surgical, postmortem and roentgenologic, or rested on clinical observation and physical examination. In 16 of the 18 cases the obstruction occurred before anthelmintic treatment was instituted. In 2 cases the obstruction occurred following treatment with santonin or with carbon tetrachloride.

Most of the patients with ascariasis were treated with hexylresorcinol or oil of chenopodium. No post-treatment obstruction resulted from the use of these anthelmintics in any of the cases.

In 6 cases with obstruction the patient died. In 4 of these cases the obstruction occurred prior to anthelmintic treatment, while in the remaining 2 it occurred following treatment (santonin, carbon tetrachloride). Since this series of cases is selective in that it does not include mild and asymptomatic ascariasis or ascariasis complicated by other diseases, the frequency of occurrence of intestinal obstruction in this series should not be construed as representative of all cases of ascariasis.

Tentative Diagnoses.—The tentative diagnoses for all cases in this series are shown in table 10. In some cases more than one tentative diagnosis was suggested. The numerous and varied diagnoses, which were made only in 1 or 2 cases each, appeared more frequently in the upper age group, in which ascariasis would be less expected.

TABLE 10.—*Tentative Diagnoses*

	No. of Patients		No. of Patients
Intestinal parasites (helminthiases)	117	Chronic bacillary dysentery	2
Ascaris infection	42	Amebiasis	2
Chronic recurrent appendicitis	35	Typhoid	2
Infection of upper respiratory tract	18	Peptic ulcer	2
Gastroenteritis (chronic or acute)	16	Duodenal ulcer	2
Tuberculosis	10	Gastrointestinal cancer	2
Intestinal obstruction due to Ascaris	7	Psychoneurosis	2
Intestinal obstruction	7	Malaria	2
Subacute appendicitis	7	Secondary anemia	2
Epilepsy	7	Neurocirculatory asthenia	1
Intussusception	6	Malnutrition	1
Intestinal intoxication	6	Gastric neurosis	1
Convulsions	4	Toxic hepatitis	1
Pyelitis	4	Biliary tract disease	1
Pneumonia	3	Hyperthyroidism	1
Chronic constipation	3	Chronic nephritis	1
Cholecystitis	3	Asthma	1
Acute appendicitis	2	Hepatic abscess	1
Chronic mesenteric lymphadenitis	2	Not given	9

Laboratory Data.—As previously noted, either the ova of A. lumbricoides or the adult worms or both were demonstrated in all cases. The infections, in general, were heavy. Cases in which there were other helminths, with the exception of a few light infections with Trichuris trichiura were excluded. No pathogenic protozoa were identified.

Total red cell counts and hemoglobin determinations were done in only a small number of the cases, in which there apparently was an indication for the procedures. In a relatively high percentage of these cases the red cell counts and the hemoglobin values were below normal (table 11). However, the cases in which the determinations were made represent a relatively small proportion of the entire series and possibly do not constitute a representative group.

In 14 of 64 cases in which total and differential leukocyte counts were made the total count exceeded 10,000 per cubic millimeter. In only 4 cases did the total leukocyte count exceed 15,000. In 15 cases the polymorphonuclear leukocytes were above 70 per cent. In 16 of the 64

TABLE 11.—*Studies of the Blood*

Total Red Blood Corpuscles per Cu. Mm.	Patients, No.	Hemoglobin	Patients, No.	Total White Blood Corpuscles per Cu. Mm.	Patients, No.
2,000,000 to 2,900,000	2	40 to 49 per cent....	1	Less than 5,000.....	4
3,000,000 to 3,900,000	10	50 to 59 per cent....	2	5,000 to 7,500.....	13
4,000,000 to 4,900,000	13	60 to 69 per cent....	5	7,600 to 10,000.....	33
5,000,000+.....	5	70 to 79 per cent....	6	10,000 to 15,000.....	10
		80 to 89 per cent....	8	Over 15,000.....	4
Total patients.....	30		22		64

cases the lymphocyte count was above 40 per cent. In 34 cases the lymphocytes exceeded 30 per cent. In 36 cases there was an eosinophil percentage below 3, while in 12 it exceeded 6 per cent. The maximum eosinophil count was 28 per cent.

TABLE 12.—*Differential Counts*

Polymorphonuclears	Patients, No.	Lymphocytes	Patients, No.	Eosinophils	Patients, No.
Less than 40 per cent	5	Less than 20 per cent	7	0 per cent.....	16
40 to 50 per cent.....	6	20 to 30 per cent.....	23	1 to 2 per cent.....	20
51 to 60 per cent.....	17	31 to 40 per cent.....	18	3 to 6 per cent.....	16
61 to 70 per cent.....	21	41 to 50 per cent.....	11	7 to 10 per cent.....	5
71 to 80 per cent.....	12	51+ per cent.....	5	11 to 20 per cent.....	5
81+ per cent.....	3			21+ per cent.....	2

SUMMARY

An analysis of the cases of 202 hospitalized patients with clinically evident ascariasis is presented.

Of the 202 patients, 170 were under 16 years of age. Thirty-three were children 2 years of age. Fifteen patients were over 30 years of age, which indicates the necessity for the clinical consideration of ascariasis in adults. Negro patients represented about 30 per cent of the entire group. The number of males and that of females were approximately equal. There was no apparent seasonal incidence of the cases, as the distribution based on the month of admission was fairly uniform.

The most common chief complaints, symptoms and physical findings, in order of their frequency of occurrence, were as follows: abdominal pain or discomfort, passing of ascarids prior to treatment (by anus, mouth or nose), vomiting, abdominal or epigastric tenderness, fever,

constipation, abdominal distention, cough or cold, nausea, headache and diarrhea. Convulsions, abnormal pulmonary conditions, anorexia, loss of weight, weakness, malaise, restlessness, abdominal rigidity, palpable abdominal mass, dyspepsia and dyspnea ranked next in order of frequency. Abdominal pain was often epigastric or umbilical in location, although in a significant number of cases the pain was referable to the lower part of the abdomen. It was frequently sudden in onset and recurrent in nature. In about one third of the group, the symptoms were evident for a week or less prior to admission. In about an equal number of cases the complaints which brought the patients to the hospital had been experienced intermittently for more than three months, sometimes for several years in either persistent or repeated infections.

In 18 cases the diagnosis was intestinal obstruction due to A. lumbricoides. In 16 cases the obstruction occurred prior to anthelmintic treatment. In 2 cases the obstruction occurred following treatment with santonin or with carbon tetrachloride. In both cases the termination was fatal. No post-treatment obstruction resulted in any of the cases of ascariasis in which the treatment was with hexylresorcinol or with oil of chenopodium U. S. P. In 6 cases of intestinal obstruction the patients died. Since this series included only cases of hospitalized patients with clinically evident ascariasis and thus excluded instances of mild and asymptomatic ascaris infections and those complicated by other diseases and other parasitic infections, the number of cases of intestinal obstruction in this series should not be interpreted as indicative of its frequency of occurrence in ascaris infections in general.

The most frequent tentative diagnoses included the following: intestinal parasites (helminthiases), ascaris infection, chronic recurrent appendicitis, infection of the upper respiratory tract, gastroenteritis, tuberculosis, intestinal obstruction, subacute appendicitis, epilepsy, intussusception and intestinal intoxication.

In over one half of the cases in which differential leukocyte counts were done there was an eosinophil count of less than 3 per cent. The maximum eosinophil count was 28 per cent.

HUMAN INFECTIONS WITH SALMONELLA PANAMA

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SALMONELLA panama is one of the more uncommon causes of human salmonellosis. In the surveys of Seligmann and his co-workers,[1] Borman and associates,[2] Edwards and Bruner,[3] Rubenstein and others[4] and Morris, Brim and Sellers,[5] a total of 2,798 isolations of Salmonella organisms was recorded. Of these, only 82, or 3 per cent, were S. panama. We were able to find published reports, however, of 101 established cases, excluding those of carriers, in addition to the unspecified number of cases occurring in the outbreak described by Wood and his co-workers.[6] To this total may now be added more than 100 cases which occurred in the recent Michigan outbreak, to be reported by Leeder.[7] The large majority of recorded infections caused by S. panama have been reported during the last few years; but it is impossible to say whether the apparent increase is due to greater incidence or to improved diagnostic facilities.

The purpose of this communication is to report 3 additional cases which the present authors have observed and to suggest that S. panama is not primarily an animal pathogen, which is the generally accepted view, but essentially a human parasite.

Whereas most varieties of Salmonella are of animal origin, three types —Salmonella typhi (Eberthella typhosa), Salmonella paratyphi A and Salmonella paratyphi B, are associated entirely or predominantly with human infections. Hitherto, S. panama has been considered a member of the "animal" group, as stated by Edwards and Bruner,[3] who neverthe-

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1. Seligmann, E.; Saphra, I., and Wassermann, M.: Am. J. Hyg. **38**:226, 1943.
2. Borman, E.; Wheeler, K.; West, D., and Mickle, F. L.: Am. J. Pub. Health **33**:127, 1943.
3. Edwards, P. R., and Bruner, D.: J. Infect. Dis. **72**:58, 1943.
4. Rubenstein A.; Feemster, R., and Smith, H.: Am. J. Pub. Health **34**:841, 1944.
5. Morris, J.; Brim, A., and Sellers, T.: Am. J. Pub. Health **34**:1277, 1944.
6. Wood, W. H., Jr.; Mayfield, F. H., and Frisch, A. W.: Meningitis Due to Salmonella Panama, J. A. M. A. **128**:868 (July 21) 1945.
7. Leeder, F. S.: Personal communication to the authors, 1945.

less have added: "In the present work [survey] S. panama was found rarely in animals but occurred rather frequently in man. . . ." Of 34 cultures in their series, 27 originated from man, 6 from fowls and 1 from swine.

In this connection, however, it is pertinent to mention some unpublished figures obtained from a cooperative study made by one of us (E.H.S.) and the Microbiological Research Division of the United States Department of Agriculture. Almost 2,000 strains of Salmonella were isolated from 5,190 samples of spray-dried egg powder. Only one of these was S. panama, an incidence of 0.05 per cent. It is unlikely, therefore, that contact with fowl can account for an appreciable number of human infections with this organism. Furthermore, we are not aware of any case of human infection which was attributed to animal contact.

On the other hand, transmission of infection from human beings was established, or strongly suspected, in the cases reported by Morris, Brim and Sellers [8] and by Rubenstein and his co-workers.[4] Leeder [7] stated that human transmission was probably responsible for each of the 100 or more cases included in his epidemiologic study. Of particular interest is the outbreak reported by Wood and his co-workers,[6] in which a food handler in the hospital milk laboratory was found to be a carrier. That the S. panama carrier state may be relatively frequent is suggested by the finding, in this outbreak, of 3 infants still harboring S. panama several months after the initial infection. The patient studied by Walters and his associates [9] became a chronic carrier, and Stone [10] found 3 carriers of S. panama among 2,000 food handlers in Panama. Since only 5 typhoid carriers were detected in this same group of food handlers, the incidence of carriers of S. panama may approximate that of S. typhi. We believe, therefore, that the search for the source of infections with S. panama in man should be directed toward the establishment of a direct human contact or, in the event food is incriminated, toward human, rather than animal, contamination.

Schiff [11] was the first to report S. panama infection in infants and to emphasize its serious nature in the very young. This point of view received support from the studies of Seligmann and his group,[1] from those of Wood and his associates,[6] and especially from those of Leeder,[7] in whose series 10, or about 10 per cent, contracted fatal meningitis. As far as we are aware, all of the recorded fatalities resulting from infection with S. panama have occurred in infants under 3 months of age.

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8. Sellers, T.: Personal communication to the authors, 1945. Morris, Brim and Sellers.[5]

9. Walters, H.; Appleyard, J., and Schrack, W.: Pennsylvania M. J. **48**:577, 1945.

10. Stone, W. S.: Am. J. Pub. Health **33**:706, 1943.

11. Schiff, F.: Salmonella Panama: Occurrence in Serious Infections of Infants in New York City, J. A. M. A. **111**:2458 (Dec. 31) 1938.

The clinical nature of human S. panama infection is similar to that of salmonella infection in general, a subject comprehensively discussed by Bornstein.[12] A classification of the recorded cases of S. panama infection has been made according to the terminology of that author, and the summary appears in table 1. Salmonella fever is characterized by generalized infection without obvious secondary localization; septicemia, by localized pyogenic infection, presumably blood-borne, e. g. meningitis or osteomyelitis.

Clinical Nature of S. Panama Infections

Gastroenteritis [13]	56
Salmonella fever [14]	15
Septicemia	
Meningitis [15]	16
Miscellaneous [16]	4
Nature not specified [1]	5
No data [17]	115
Total approximately	211

S. PANAMA GASTROENTERITIS

The most frequent clinical manifestation of S. panama infection is gastroenteritis. This form of the disease usually produces mild symptoms in adults, but it may be fatal in infants.[9] An instance of a mild S. panama gastroenteritis is reported (case 1).

CASE 1.—Mrs. E. M., a 25 year old white nullipara, gave birth to a normal, full term infant on Feb. 8, 1945. Twenty-four hours post partum, she passed three liquid stools, and two hours later she had a chill, followed by a rise in

12. Bornstein, S.: J. Immunol. **46**:439, 1943.

13. Jordan, E. O.: J. Infect. Dis. **55**:224, 1934. Preuss, H.: Zentralbl. f. Bact. (Abt. 1) **141**:94, 1941. Haedo, A., and Devincenzi, R.: An. Fac. de med. de Montevideo **27**:449, 1942. Seligmann, E., and Hartz, J. J.: Ann. Int. Med. **20**:743, 1944. Levine, M., and Smith, B. A.: Minnesota Med. **24**:966, 1941. Seligmann, Saphra and Wassermann.[1] Edwards and Bruner.[3] Rubenstein, Feemster and Smith.[4] Morris, Brim and Sellers.[5] Wood, Mayfield and Frisch.[6] Sellers.[8]

14. Seligmann, Saphra and Wassermann.[1] Edwards and Bruner.[3] Rubenstein, Feemster and Smith.[4] Morris, Brim and Sellers.[5] Walters, Appleyard and Schrack.[9]

15. (a) Katsampes, C., and Bradford, W.: J. Pediat. **16**:79, 1940. (b) Seligmann, Saphra and Wassermann.[1] (c) Edwards and Bruner.[3] (d) Wood, Mayfield and Frisch.[6] (e) Leeder.[7] (f) Leeder, in a personal communication, stated that 10 deaths in his series were attributable to S. panama meningitis. The number of cases in which the disease was not fatal is not known to us.

16. Seligmann, E.: Personal communication to the authors, 1945. Seligmann, Saphra and Wassermann.[1]

17. Approximately 100 cases which Leeder stated will be described in a forthcoming publication. Leeder.[7] Seligmann, Saphra and Wassermann.[1] Borman, Wheeler, West and Mickle.[2] Rubenstein, Feemster, and Smith.[4] Morris, Brim and Sellers.[5] Walters, Appleyard and Schrack.[9]

temperature to 102 F., although the pulse rate was only 90 beats per minute at this time. She was immediately removed from the obstetric unit, with a provisional diagnosis of typhoid, since a mild epidemic of that disease was present in the Philadelphia area.

She never appeared to be extremely ill. Within forty-eight hours her temperature had returned to normal, and within five days from the onset her stools were also normal. She received sulfadiazine by mouth, in doses of 0.5 Gm. every four hours, after S. panama was isolated from her stools. A total of 10 Gm. of this drug was given. Symptomatic antidiarrheal therapy was also used. At the time of her discharge from the hospital, on February 17, no unusual conditions were noted. Her infant had been exposed at three nursing periods before the onset of her symptoms, but never showed evidence of infection.

Bacteriologic Data.—Mrs. E. M.: A blood culture taken on February 10 failed to reveal the organism, but a fecal swab culture yielded S. panama. A rectal swab culture made showed the organism on February 17, but one made on March 11 did not. No specific agglutinins were present in serums collected on February 10 and February 14, but by February 17 H and O agglutinin titers of 1 to 160 were obtained. Another test on March 11 gave the same results.

Baby M.: Two fecal cultures, one on February 17 and another on March 11, failed to show S. panama, and serum collected on February 17 did not contain specific agglutinins.

Tests of Susceptibility to Sulfonamide Compounds.—Inhibition of growth of the homologous strain of S. panama was determined in inhibitor-free broth, using an inoculum of 1,500 cells from an eighteen hour culture. The results showed that sulfadiazine and sulfathiazole inhibited the organisms at dilutions of 1 to 4,000. Sulfapyridine sodium, however, was not effective at dilutions above 1 to 1,000, and sulfanilamide was not bacteriostatic in a concentration of 1 to 500.

S. PANAMA SEPTICEMIA

Twenty-five cases of S. panama septicemia or localized pyogenic infection due to S. panama have been reported. Sixteen of these were meningitis; the remainder were miscellaneous infections.

Thirteen of the 16 reported cases of meningitis were fatal. The ages were recorded in 5 instances and ranged from 3 weeks to 3 months. Sulfadiazine therapy was employed in 1 of the fatal cases and also in 2 cases of infants that survived. The other recovery was of an infant who received sulfapyridine. The patient described in the following report was an infant successfully treated with sulfadiazine.

CASE 2.—Fever suddenly developed in S. D., a 2½ month old white boy, on June 28, 1944, and he had a generalized convulsive seizure which lasted thirty minutes. He was promptly admitted to a small emergency hospital, where he remained in a critical condition for two weeks. During this time sulfadiazine was administered empirically. The cause for his illness was obscure until July 17, when a diagnosis of meningitis was made, and he was referred to Temple University Hospital for further study and treatment.

Nothing significant was noted in his past medical history. There was no illness in the patient's family at the time, and no epidemic of intestinal infections in the community. Physical examination revealed an acutely ill, pale and hyperirritable infant, whose rectal temperature was 102.8 F. There were signs of meningeal and cerebral irritation.

Lumbar puncture was performed immediately and yielded grossly cloudy fluid. A diagnosis of purulent meningitis was made, and he was given sulfadiazine orally, 0.5 Gm. at once, followed by 0.25 Gm. every six hours. Alkalis were likewise given, together with generous amounts of fluid. This dose of sulfadiazine was sufficient to produce a blood level of 11 to 18 mg. per hundred cubic centimeters. In ten hours his temperature dropped to normal, and, except for an occasional rise to 100 F. (rectally) during the first sixty hours, it remained normal thereafter. Twelve hours following admission, the lumbar puncture was repeated. From this fluid and from that obtained on admission, the causative organism was recovered. Four subsequent specimens of cerebrospinal fluid, including one obtained by cisternal puncture, were sterile. The infection subsided gradually, and on July 22 the dose of sulfadiazine was reduced to 0.13 Gm. every six hours. This was discontinued on August 3 without recurrence of symptoms. He was discharged from the hospital on August 15, free of infection, but with residual deafness, blindness and partial paralysis of his right arm and forearm. On December 14, a pneumoencephalogram showed moderate communicating hydrocephalus. Obliteration of the subarachnoid pathways was noted, with air present only in the basilar cisterns. These changes were thought to be secondary to postmeningitic basilar arachnoiditis.

He has been examined five times at approximately three month intervals since discharge from the hospital. His growth has been normal, although he has retained the residuals of his infection. When last seen, sixteen months after the acute episode, he was slowly improving but was still obviously retarded.

Bacteriologic Data.—Two specimens of cerebrospinal fluid collected on July 17 yielded S. panama, but successive ones, on July 19, 24 and 31 and August 4, did not. This organism was not recovered from throat cultures made on July 17 and 19 or from a blood culture on July 17, or from fecal swabs on July 22—(3 specimens). Cultures made from rectal swabs made on March 4, 1945 also failed to reveal the organism.

No specific agglutinins were detected in the patient's serum on July 21, but by August 1 H and O titers of 1 to 640 were obtained. Repeat tests showed persistence of the antibody, since the titer on December 16 was 1 to 160. By March 4, 1945, however, the H titer was 1 to 20 and the O titer less than that. No agglutinins were detected on June 24, 1945. Reactions to tests for spinal fluid agglutinins on July 20, 1944 and on Dec. 16, 1944 were both negative.

Tests of Susceptibility to Sulfonamide Compounds.—The results of growth inhibition tests in inhibitor-free broth, with an inoculum of 1,500 cells of the homologous strain, showed that both sulfathiazole and sulfadiazine inhibited growth at dilutions of 1 to 16,000, and sulfapyridine, at 1 to 2,000. Sulfanilamide was not bacteriostatic in a concentration of 1 to 500.

Studies of Contacts.—Rectal swab cultures from the mother, father and two sisters all failed to reveal S. panama on March 4, 1945, and specific agglutinins could not be demonstrated in their serums at this time.

PERITONITIS AND PNEUMONITIS

The following case is one of interstitial pneumonitis and peritonitis in a newborn infant who died at the age of 4 days. The source of infection was not established.

CASE 3.—On Dec. 4, 1944, Mrs. W., a 28 year old white multipara, was admitted to Temple University Hospital for induction of labor, because serial

anti-Rh agglutination studies showed rising titers. Her previous pregnancy had been uneventful. On December 4 and December 7, unsuccessful attempts were made to induce labor. On December 8, a Vorhees bag was inserted into the uterus without effect. This was repeated on December 10, and after a short labor a 6 pound 5 ounce (2,863 Gm.) girl was delivered spontaneously.

The infant was examined carefully and showed no clinical or laboratory evidence of erythroblastosis fetalis. The infant's first three days of life were uneventful except for moderate, but not alarming, loss of weight. On the fourth day the infant weighed only 5 pounds 7 ounces (2,522 Gm.), representing a loss of 13.8 per cent from her birth weight. Her rectal temperature was 103 F. She was apathetic, her respirations were labored and she appeared critically ill. Moderate icterus and dehydration were present. Over the lower part of the abdomen there was a red, slightly indurated eruption, distributed in a butterfly pattern from the umbilicus to the pubis. The abdomen was distended, but peristalsis could be heard. Poor air exchange was noted at the bases of both lungs. Results of a neurologic examination were negative; the fontanels were depressed.

A diagnosis of sepsis was made, but before any therapy could be undertaken the infant died. The postmortem examination was performed twenty hours after death. The eruption on the lower part of the abdomen was still present. The most significant findings were atelectasis of the lower lobes of both lungs, with considerable bronchiolar exudate; a dense, fibrinous exudate in the abdominal cavity, chiefly around the liver and spleen, and severe congestion of the large and the small intestine. There was no gross evidence of erythroblastosis fetalis.

Microscopic sections of the lungs showed acute ulcerative bronchiolitis, with early interstitial pneumonitis. The intestinal tract showed acute inflammatory changes, most pronounced in the ileum. Shallow ulcerations marked the mucosal surface, particularly in the region of Peyer's patches. There was no histologic evidence of erythroblastosis fetalis. The placenta was normal, as shown by gross and microscopic examinations. The gross and histologic observations suggest that the infection was of at least forty-eight hours' duration, and could have occurred at birth.

Bacteriologic Data.—Baby W.: Antemortem and postmortem blood cultures were overgrown with Proteus vulgaris; a postmortem culture from the diaphragmatic surface was similarly overgrown with Pseudomonas pyocyanea. Swabs from the gallbladder area and swabs of bronchiolar exudate, however, contained pure cultures of S. panama. It is not unreasonable to presume that S. panama was present in all the cultures, since growth of Proteus and Pseudomonas is such as to mask the presence of other bacterial colonies, and selective agents for the cultural separation of Salmonella from Proteus and Pseudomonas are not available.

Mrs. W.: Nine weeks after the delivery, fecal cultures and serum agglutinin tests were made, but both failed to reveal S. panama.

Regardless of the fact that the isolation of S. panama from animals is relatively infrequent, Edwards and Bruner [3] expressed the opinion that this organism is primarily an animal pathogen. We disagree with this point of view, since the recorded isolations have been made almost exclusively from human beings; and we believe that S. panama should be regarded as a "human" type of Salmonella, along with S. typhi, S. paratyphi A and S. paratyphi B.

Although the possibility of animal-to-man transmission cannot be disregarded, this mode of infection seems highly improbable in most instances of human infection, especially with respect to newborn infants. In our opinion the infected human being or the asymptomatic carrier is the more likely source.

Salmonella infections of the female genital tract have been reported.[18] Furthermore, Watt and Carlton[19] described a small outbreak of Salmonella typhi murium infection among newborn infants, which originated from a woman who undoubtedly was infected with this organism at the time of delivery. In our case 3 there is no proof of a maternal infection. But the facts that there were no other cases of S. panama infection in the institution at the time, that the onset was only three days after birth and that the pathologic findings indicated a process of at least two days' duration suggest that the mother may have been the source of infection. Unfortunately, we were unable to examine the mother bacteriologically until nine weeks later. At this time fecal cultures and serum agglutinin tests failed to reveal the presence of S. panama. The obstetric manipulations in this case would, of course, increase the possibility of infection.

From the results of the in vitro susceptibility tests with 2 of our strains, it would appear that sulfadiazine and sulfathiazole are the drugs of choice among the commonly used sulfonamide compounds. Seligmann[16] has reported the successful use of sulfadiazine in the treatment of meningitis caused by S. panama as have also Wood and his associates.[6] Since the amount of sulfathiazole and sulfadiazine required to inhibit strain E.M. was four times as great as that required to inhibit strain S.D., significant variation in susceptibility undoubtedly exists among different strains.

SUMMARY

Three cases of Salmonella panama infection are described: the first, one of mild gastroenteritis in an adult; the second, one of meningitis successfully treated with sulfadiazine in an infant, and the third, one of fatal Salmonella septicemia in a newborn infant.

Data pertaining to more than 200 cases of S. panama infection have been classified.

S. panama should be considered as primarily a "human" type of Salmonella, the transmission of which is predominantly from man to man rather than from animal to man.

18. Falk, H. C., and Blinick, G.: Am. J. Obst. & Gynec. **47**:514, 1944.
19. Watt, J., and Carlton, E.: Pub. Health Rep. **60**:734, 1945.

The severe nature of infections with this organism in young infants is discussed, and the possibility of transmission from mother to infant is emphasized.

In vitro tests suggest that sulfadiazine or sulfathiazole is the sulfonamide compound of choice, although different strains must be expected to vary significantly in their response to either drug.

Dr. E. S. Gault, Department of Pathology of Temple University Hospital furnished the report and the interpretation of the postmortem examination.

CAUSES OF PREMATURITY

VIII. Influence of Infections, Chronic Disorders and Accidents on the Incidence of Prematurity

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IN PREVIOUS reports the association of maternal syphilis, toxemia and uterine bleeding with the incidence of premature delivery has been investigated. There remains a number of other infections and chronic disorders less frequently encountered during pregnancy which may have an influence on the length of the gestation period. Certain conditions, such as tuberculosis and heart disease, have been singled out by other authors as specific factors contributing to premature delivery. In 13 reports in the literature [1] the incidence of tuberculosis among the mothers of premature infants varied from 0.2 to 5.5 per cent. Fourteen authors observed that the incidence of heart disease among mothers of premature infants ranged from 0.1 to 8.3 per cent. Other acute and chronic conditions noted by seventeen authors were found to occur in percentages varying from 1.4 to 16.3.

The incidence of these diseases in our series of 13,526 mothers and infants was too low to permit the detailed analysis employed in our previous reports, but by grouping similar types of illnesses we have arrived at an estimate of their relative importance as predisposing factors of premature delivery.

DEFINITIONS AND PROCEDURES

The methods of collecting the data and the definitions of prematurity and of stillbirth which have been employed are the same as described in a previous report.[2]

The diagnosis of the illnesses described in this paper had generally been made by a physician in the prenatal clinic or by a member of the

From the Children's Hospital Research Foundation and the Department of Pediatrics, University of Cincinnati College of Medicine.

1. Anderson, N. A., and Lyon, R. A.: Causes of Prematurity: I. Review of the Literature, Am. J. Dis. Child. **58**:586 (Sept.) 1939.

2. Brown, E. W.; Lyon, R. A., and Anderson, N. A.: Causes of Prematurity: IV. Influence of Maternal Illness on the Incidence of Prematurity; Employment of a New Criterion of Prematurity for the Negro Race, Am. J. Dis. Child. **70**:314 (Nov.-Dec.) 1945.

hospital staff, from clinical and laboratory evidence obtained after the patient entered the hospital for delivery. In some instances the history given by the mother was sufficiently specific or characteristic to be accepted as accurate evidence of a definite illness suffered during the period of her pregnancy.

OBSERVATIONS

Acute Infections.—The diseases included in the group of acute infections were those infections believed to be caused by the invasion of bacteria or viruses. Syphilis was not included because its influence had been discussed in detail in a previous report.[3] The classification was not entirely satisfactory because the diseases varied so greatly in severity and in duration. Diseases of the respiratory and of the genitourinary tracts were predominant, but only by a consideration of the individual infections as causes of prematurity can a true picture of their influence be determined.

No single type of infection occurred with sufficient frequency in this series to permit such detailed analysis. It seemed impractical, therefore, to separate into groups the patients who had each disease as the sole abnormality of pregnancy and those who had additional diseases which might have contributed to premature delivery.

A total number of 412 white women had acute infections during pregnancy, and 13.8 per cent of this group gave birth to premature infants (table 1). This rate of premature delivery was well above 5.5 per cent, the rate of the women who had entirely normal pregnancies. A total number of 326 Negro women had acute infections during pregnancy, and 20.6 per cent of their infants were born prematurely, as compared with 9.2 per cent of the offspring of Negro women whose pregnancies were unmarred by disease or other abnormal conditions (table 2). As in previous reports, the standard of prematurity of Negro infants was then adjusted to include only those whose birth weights were less than 5 pounds, 3 ounces (2,350 Gm.); a category more comparable to the white infants in respect to the stage of development. With such a standard the incidence of prematurity among the offspring of Negro women with acute infections was 15.3 per cent, a rate not greatly different from that of the white race (table 3).

Pulmonary Tuberculosis: Eighty-one white women had pulmonary tuberculosis and 14.8 per cent of them had premature infants. The stage of the disease could not always be determined with accuracy, but in 17 of the mothers of live-born infants the disease proved to be active.

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3. Brown, E. W.; Lyon, R. A., and Anderson, N. A.: Causes of Prematurity: V. Influence of Syphilis on the Incidence of Prematurity, Am. J. Dis. Child. **70:** 318 (Nov.-Dec.) 1945.

TABLE 1.—*The Incidence of Premature Births to Women with Acute Infections (Single Births Only)*

White Race—Criterion of prematurity: birth weight less than 5 pounds 8 ounces (2,500 Gm.)

Infection	Live-Born			Stillborn			Live-Born and Stillborn		
	Premature	Full Term	Total	Premature	Full Term	Total	Premature	Full Term	Total
Tuberculosis	10 (13%)	68	78	2 (67%)	1	3	12 (15%)	69	81
Pneumonia	5 (25%)	15	20	0	1	1	5 (24%)	16	21
"Influenza"	1 (1%)	89	90	0	0	0	1 (1%)	89	90
Contagious disease	2 (11%)	16	18	1 (50%)	1	2	3 (15%)	17	20
Rheumatic fever	0	3	3	0	0	0	0	3	3
Arthritis—other forms	2 (15%)	11	13	0	0	0	2 (15%)	11	13
Otitis media	0	6	6	1 (100%)	0	1	1 (14%)	6	7
Pyelitis	6 (11%)	48	54	2 (100%)	0	2	8 (14%)	48	56
Gonorrhea, pelvic disease	18 (25%)	54	72	1 (33%)	2	3	19 (25%)	56	75
Abscesses	0	15	15	0	0	0	0	15	15
Jaundice—catarrhal	2 (40%)	3	5	1 (100%)	0	1	3 (50%)	3	6
Other severe infections	2 (100%)	0	2	0	0	0	2 (100%)	0	2
Minor infections	0	22	22	1 (100%)	0	1	1 (4%)	22	23
Total	48 (12%)	350	398	9 (64%)	5	14	57 (14%)	355	412

TABLE 2.—*The Incidence of Premature Births to Women with Acute Infections (Single Births Only)*

Negro Race—Criterion of prematurity: birth weight less than 5 pounds 8 ounces (2,500 Gm.)

Infection	Live-Born			Stillborn			Live-Born and Stillborn		
	Premature	Full Term	Total	Premature	Full Term	Total	Premature	Full Term	Total
Tuberculosis	13 (19%)	55	68	0	1	1	13 (19%)	56	69
Pneumonia	0	7	7	1 (100%)	0	1	1 (12%)	7	8
"Influenza"	5 (14%)	30	35	1 (100%)	0	1	6 (17%)	30	36
Contagious disease	2 (22%)	7	9	0	0	0	2 (22%)	7	9
Rheumatic fever	0	2	0	0	0	0	0	2	2
Arthritis—other forms	7 (35%)	13	20	2 (100%)	0	2	9 (41%)	13	22
Pyelitis	7 (21%)	26	33	0	1	1	7 (21%)	27	34
Gonorrhea—pelvic infections	20 (19%)	86	106	3 (60%)	2	5	23 (21%)	88	111
Abscesses	0	4	4	0	0	0	0	4	4
Osteomyelitis	1 (12%)	7	8	0	0	0	1 (12%)	7	8
Jaundice—catarrhal	0	1	1	0	0	0	0	1	1
Minor infections	5 (24%)	16	21	0	1	1	5 (23%)	17	22
Total	60 (19%)	254	314	7 (58%)	5	12	67 (21%)	259	326

Three of the offspring of these patients were prematurely born. Among the Negro mothers 69 had tuberculosis, and 18.8 per cent of their offspring were classed as premature infants when 5 pounds, 8 ounces (2,500 Gm.) was employed as a standard of prematurity while 17.4 per cent were premature under the adjusted classification. All of these rates were well above those of normal patients. Tuberculosis was in its active stages in 10 of the Negro patients, and 5 of the offspring of these mothers weighed less than 5 pounds, 8 ounces (2,500 Gm.) at birth.

The remaining group of white and Negro women had arrested pulmonary tuberculosis. Many had been patients in a tuberculosis sanatorium. The histories of all of the previous pregnancies of these patients were reviewed to see whether there had been a high incidence of prematurity among previous offspring when the tuberculous process of their mother was probably active, but the prematurity rates in these families did not seem abnormally high.

Pneumonia: Twenty white patients and only 8 Negro patients had pneumonia. Among the white women the disease was associated with a higher rate of premature deliveries (24 per cent) than among the Negro women (12.5 per cent). The latter rate represented only 1 premature birth among the offspring of the Negro mothers.

"Influenza": This term was applied to severe infections of the upper respiratory tract accompanied with systemic symptoms which persisted for several days. Ordinary colds were not recorded. The prematurity rate among the offspring of white patients with this disease was only 1 per cent, and among the two categories of offspring of Negro patients the rates were 17 per cent and 14 per cent respectively.

Contagious Diseases: These included measles, German measles, pertussis, chickenpox and mumps. The incidence of prematurity among the offspring of the women of both races who had these infections was approximately 15 per cent. The most frequent contagious disease was measles, which occurred in 8 white and 2 Negro mothers. In 1 white mother this infection occurred during the sixth month of pregnancy, and it was followed by the delivery of a premature infant weighing 2 pounds, 6 ounces, (1,027 Gm.) who died shortly after birth. In the other patients the attack of measles occurred at periods varying from the fourth to the ninth month of pregnancy, and the disease seemed to have no influence in causing premature delivery or in impairing the health of the infant.

German measles occurred in 3 patients at periods varying from the fifth to the eighth month of pregnancy, but all of their offspring were normal and were delivered at term.

Mumps occurred in 8 patients, but in only one instance was there a possibility that the disease, which developed in the eighth month of preg-

TABLE 3.—*The Incidence of Premature Births to Women with Acute Infections (Single Births Only)*

Negro Race—Criterion of prematurity: birth weight less than 5 pounds 3 ounces (2,350 Gm.)

Infection	Live-Born			Stillborn			Live-Born and Stillborn		
	Premature	Full Term	Total	Premature	Full Term	Total	Premature	Full Term	Total
Tuberculosis	12 (18%)	56	68	0	1	1	12 (17%)	57	69
Pneumonia	0	7	7	1 (100%)	0	1	1 (12%)	7	8
"Influenza"	4 (11%)	31	35	1 (100%)	0	1	5 (14%)	31	36
Contagious disease	1 (11%)	8	9	0	0	0	1 (11%)	8	9
Rheumatic fever	0	2	2	0	0	0	0	2	2
Arthritis—other forms	7 (35%)	13	20	2 (100%)	0	2	9 (41%)	13	22
Pyelitis	5 (18%)	28	33	0	1	1	5 (15%)	29	34
Gonorrhea—pelvic infection	12 (11%)	94	106	2 (40%)	3	5	14 (13%)	97	111
Abscesses	0	4	4	0	0	0	0	4	4
Osteomyelitis	0	8	8	0	0	0	0	8	8
Jaundice—catarrhal	0	1	1	0	0	0	0	1	1
Minor infections	3 (14%)	18	21	0	1	1	3 (14%)	19	22
Total	44 (14%)	270	314	6 (50%)	6	12	50 (15%)	276	326

TABLE 4.—*The Incidence of Premature Births to Women with Chronic Disorders (Single Births Only)*

White Race—Criterion of prematurity: birth weight less than 5 pounds 8 ounces (2,500 Gm.)

Chronic Disorders	Live-Born			Stillborn			Live-Born and Stillborn		
	Premature	Full Term	Total	Premature	Full Term	Total	Premature	Full Term	Total
Heart disease	10 (11%)	81	91	5 (100%)	0	5	15 (16%)	81	96
Hypertension	1 (17%)	5	6	0	0	0	1 (17%)	5	6
Nephritis	0	6	6	3 (100%)	0	3	3 (33%)	6	9
Cholecystitis, chronic	1 (10%)	9	10	0	0	0	1 (10%)	9	10
Goiter or past thyroidectomy	1 (3%)	30	31	1 (100%)	0	1	2 (6%)	30	32
Diabetes	2 (25%)	6	8	0	0	0	2 (25%)	6	8
Cancer	1 (33%)	2	3	0	0	0	1 (33%)	2	3
Asthma	2 (6%)	33	35	0	1	1	2 (6%)	34	36
Anemia	1 (8%)	11	12	0	1	1	1 (8%)	12	13
Mental disorder	7 (10%)	66	73	0	0	0	7 (10%)	66	73
Other conditions	14 (10%)	120	134	2 (67%)	1	3	16 (12%)	121	137
Total	40 (10%)	369	409	11 (79%)	3	14	51 (12%)	372	423

nancy, may have been responsible for the early delivery of a slightly underweight (5 pound, 2 ounce) (2,325 Gm.) infant.

Chickenpox occurred in 4 patients. One mother who contracted this illness was soon delivered of an infant weighing 3 pounds, 8 ounces (1,534 Gm.).

Whooping cough occurred in 4 patients at periods varying from the fourth to the seventh month of pregnancy. None of these women had premature or abnormal infants.

Pyelitis: This disease was associated with premature delivery in 14 per cent of the white mothers. In the two categories of Negro offspring the rates were 21 and 15 per cent respectively.

Gonorrhea: This disease was recorded only when the infection was sufficiently acute to produce definite symptoms or signs of illness. Probably many other patients had latent forms of the disease. A total number of 75 white women had acute forms of the disease, and 25 per cent of their offspring were prematurely born. Among the 111 Negro patients with acute manifestations, prematurity rates of the offspring in the two categories were 21 and 13 per cent respectively.

Other infections, which occurred less frequently, are listed in the accompanying tables. Severe infections included such diseases as osteomyelitis and dysentery. Among the minor infections were numerous cutaneous diseases and superficial infections which caused no systemic reactions.

Chronic Disorders.—Chronic disorders occurred in 423 white women, and 12 per cent of their offspring were prematurely born (table 4). There were 297 Negro women with similar disorders, and 15 per cent of their offspring were prematurely born (table 5). When prematurity in the Negro infants was restricted to those whose birth weight was less than 5 pounds, 3 ounces (2,350 Gm.), the prematurity rate fell to 11 per cent (table 6).

The diagnosis of heart disease was made from clinical observations only and not from the patients' histories. Among the offspring of 96 white patients with heart disease, 16 per cent were premature. Among the offspring of 84 Negro patients, the prematurity rate was likewise 15 per cent, and when the revised standard of prematurity was employed, the rate was 12 per cent. In the great majority of instances the heart disease had been caused by a rheumatic infection occurring some time before pregnancy. It was impossible to judge accurately the degree of cardiac damage or of circulatory insufficiency in most of these patients. In the entire group were 2 with subacute bacterial endocarditis, 3 with coronary artery disease, 1 with auricular fibrillation and 1 with paroxysmal ventricular tachycardia; all of these 7 women were delivered of full term, living infants.

TABLE 5.—*The Incidence of Premature Births to Women with Chronic Disorders (Single Births Only)*

Negro Race—Criterion of prematurity: birth weight less than 5 pounds 8 ounces (2,500 Gm.)

Chronic Disorders	Live-Born			Stillborn			Live-Born and Stillborn		
	Premature	Full Term	Total	Premature	Full Term	Total	Premature	Full Term	Total
Heart disease	12 (15%)	70	82	1 (50%)	1	2	13 (15%)	71	84
Hypertension	0	4	4	0	1	1	0	5	5
Nephritis	0	1	1	0	0	0	0	1	1
Cholecystitis, chronic	1 (100%)	0	1	0	0	0	1 (100%)	0	1
Goiter or past thyroidectomy	1 (9%)	10	11	1 (100%)	0	1	2 (17%)	10	12
Diabetes	0	5	5	0	4	4	0	9	9
Asthma	6 (18%)	27	33	1 (50%)	1	2	7 (20%)	28	35
Anemia	1 (25%)	3	4	1 (100%)	0	1	2 (40%)	3	5
Mental disorder	5 (25%)	15	20	0	0	0	5 (25%)	15	20
Other conditions	13 (11%)	105	118	2 (29%)	5	7	15 (12%)	110	125
Total	39 (14%)	240	279	6 (33%)	12	18	45 (15%)	252	297

TABLE 6.—*The Incidence of Premature Births to Women with Chronic Disorders (Single Births Only)*

Negro Race—Criterion of prematurity: birth weight less than 5 pounds 3 ounces (2,350 Gm.)

Chronic Disorders	Live-Born			Stillborn			Live-Born and Stillborn		
	Premature	Full Term	Total	Premature	Full Term	Total	Premature	Full Term	Total
Heart disease	9 (11%)	73	82	1 (50%)	1	2	10 (12%)	74	84
Hypertension	0	4	4	0	1	1	0	5	5
Nephritis	0	1	1	0	0	0	0	1	1
Cholecystitis, chronic	1 (100%)	0	1	0	0	0	1 (100%)	0	1
Goiter or past thyroidectomy	1 (9%)	10	11	1 (100%)	0	1	2 (17%)	10	12
Diabetes	0	5	5	0	4	4	0	9	9
Asthma	3 (9%)	30	33	1 (50%)	1	2	4 (11%)	31	35
Anemia	1 (25%)	3	4	1 (100%)	0	1	2 (40%)	3	5
Mental disorder	3 (15%)	17	20	0	0	0	3 (15%)	17	20
Other conditions	8 (7%)	110	118	2 (29%)	5	7	10 (8%)	115	125
Total	26 (9%)	253	279	6 (33%)	12	18	32 (11%)	265	297

Other chronic disorders occurred less frequently. Hypertension and nephritis were recorded separately from toxemia when the conditions were known to exist before the beginning of pregnancy. Anemia was listed only when it was a specific type or a severe protracted form; secondary anemia of mild degree was not included in this category. Among the mental disorders were epilepsy and various forms of psychopathic conditions. The group of "other disorders" included such conditions as uterine fibroids, deformities of the skeleton and paralysis of the muscles from poliomyelitis.

The serious influence of certain chronic infections on the outcome of pregnancy was not always clearly portrayed in the previously mentioned tables. Many mothers with chronic disorders had repeated pregnancies, and it seems probable that the underlying disease may have been smoldering for a considerable length of time during the earlier pregnancies before an accurate diagnosis was made. This situation seemed to be true among the diabetic patients. This disease was detected in 17 women of both races, and only 2 of their offspring were premature. When complete family histories were examined and the outcome of every pregnancy of these patients was analyzed, it was discovered that the incidence of stillbirth was unusually high. Among the live-born infants there were large numbers of underweight and overweight infants, who frequently died shortly after birth.

Accidents and Other Complications.—Accidental injuries, such as falls, blows, burns, automobile accidents and nonobstetric surgical operations happened to 97 white women during their pregnancies. Among their offspring, 9.3 per cent were premature infants (table 7). Among the infants of Negro mothers the prematurity rate was 18 per cent or, with the revised standard, 15 per cent (tables 8 and 9).

A total number of 88 white mothers had some complication of pregnancy, and the rate of prematurity among their offspring was 7 per cent (table 7). Among the Negro offspring the rate was 8 per cent in both classifications of prematurity (tables 8 and 9). Abdominal pain was listed separately only when it was persistent or unusually severe.

Among the offspring of 166 white patients with some abnormality of labor or delivery, the prematurity rate was 10 per cent. Among the offspring of Negro patients in this group the rates in the two categories were 13 per cent and 7 per cent.

The majority of patients in this group had difficult labor because of some disproportion between the size of the infant's head and the size of the mother's pelvic outlet. Whenever some other serious illness occurred or operative measures were employed, the patients were listed in such subgroups. Among the remaining number of patients, however, the only abnormalities were a contracted or flat pelvis, cephalo-

TABLE 7.—*The Incidence of Premature Births to Mothers with Accidents and Those with Complications of Pregnancy, Labor and Delivery (Single Births Only)*

White Race—Criterion of prematurity: birth weight less than 5 pounds 8 ounces (2,500 Gm.)

	Live-Born			Stillborn			Live-Born and Stillborn		
	Premature	Full Term	Total	Premature	Full Term	Total	Premature	Full Term	Total
Accidents									
Severe fall	4 (7%)	51	55	0	1	1	4 (7%)	52	56
Nonobstetric surgical intervention	1 (14%)	6	7	1 (100%)	0	1	2 (25%)	6	8
Other accidents	3 (9%)	30	33	0	0	0	3 (9%)	30	33
Total	8 (8%)	87	95	1 (50%)	1	2	9 (9%)	88	97
Complications of pregnancy									
Abdominal pain	2 (5%)	37	39	0	0	0	2 (5%)	37	39
Threatened abortion	0	16	16	0	0	0	0	16	16
Hydramnios	2 (25%)	6	8	0	0	0	2 (25%)	6	8
Phlebitis	0	2	2	0	0	0	0	2	2
Varicose veins	0	18	18	0	0	0	0	18	18
Other complications	2 (40%)	3	5	0	0	0	2 (40%)	3	5
Total	6 (7%)	82	88	0	0	0	6 (7%)	82	88
Complications of labor or delivery									
Abnormal pelvic measurements	3 (8%)	35	38	0	0	0	3 (8%)	35	38
Abnormal presentation	1 (6%)	16	17	2 (100%)	0	2	3 (16%)	16	19
Operative delivery	2 (3%)	66	68	0	3	3	2 (3%)	69	71
Premature rupture of membranes	1 (8%)	11	12	2 (67%)	1	3	3 (20%)	12	15
Uterine inertia	4 (40%)	6	10	0	0	0	4 (40%)	6	10
Cephalopelvic disproportion	0	0	0	0	1	1	0	1	1
Other complications	2 (17%)	10	12	0	0	0	2 (17%)	10	12
Total	13 (8%)	144	157	4 (44%)	5	9	17 (10%)	149	166

TABLE 8.—*The Incidence of Premature Births to Women with Accidents and Those with Complications of Pregnancy, Labor and Delivery—(Single Births Only)*

Negro Race—Criterion of prematurity: birth weight less than 5 pounds 8 ounces (2,500 Gm.)

	Live-Born			Stillborn			Live-Born and Stillborn		
	Premature	Full Term	Total	Premature	Full Term	Total	Premature	Full Term	Total
Accidents									
Severe fall	5 (22%)	18	23	0	0	0	5 (22%)	18	23
Nonobstetric surgical intervention	0	2	2	0	0	0	0	2	2
Other accidents	2 (14%)	12	14	0	0	0	2 (14%)	12	14
Total	7 (18%)	32	39	0	0	0	7 (18%)	32	39
Complications of pregnancy									
Abdominal pain	3 (12%)	21	24	0	0	0	3 (12%)	21	24
Threatened abortion	0	4	4	0	0	0	0	4	4
Hydramnios	1 (20%)	4	5	0	0	0	1 (20%)	4	5
Varicose veins	0	10	10	0	0	0	0	10	10
Other complications	0	5	5	0	0	0	0	5	5
Total	4 (8%)	44	48	0	0	0	4 (8%)	44	48
Complications of labor or delivery									
Abnormal pelvic measurements	7 (14%)	43	50	0	1	1	7 (13%)	44	51
Abnormal presentation	2 (29%)	5	7	0	1	1	2 (25%)	6	8
Operative delivery	4 (11%)	32	36	0	4	4	4 (10%)	36	40
Premature rupture of membranes	2 (25%)	6	8	0	0	0	2 (25%)	6	8
Uterine inertia	0	7	7	0	0	0	0	7	7
Cephalopelvic disproportion	0	0	0	0	1	1	0	1	1
Other complications	0	4	4	0	0	0	0	4	4
Total	15 (13%)	97	112	0	7	7	15 (13%)	104	119

TABLE 9.—*The Incidence of Premature Births to Women with Accidents and Those with Complications of Pregnancy, Labor and Delivery—(Single Births Only)*

Negro Race—Criterion of prematurity: birth weight less than 5 pounds 3 ounces (2,350 Gm.)

	Live-Born			Stillborn			Live-Born and Stillborn		
	Premature	Full Term	Total	Premature	Full Term	Total	Premature	Full Term	Total
Accidents									
Severe fall	4 (17%)	19	23	0	0	0	4 (17%)	19	23
Nonobstetric surgical intervention	0	2	2	0	0	0	0	2	2
Other accidents	2 (14%)	12	14	0	0	0	2 (14%)	12	14
Total	6 (15%)	33	39	0	0	0	6 (15%)	33	39
Complications of pregnancy									
Abdominal pain	3 (12%)	21	24	0	0	0	3 (12%)	21	24
Threatened abortion	0	4	4	0	0	0	0	4	4
Hydramnios	1 (20%)	4	5	0	0	0	1 (20%)	4	5
Varicose veins	0	10	10	0	0	0	0	10	10
Other complications	0	5	5	0	0	0	0	5	5
Total	4 (8%)	44	48	0	0	0	4 (8%)	44	48
Complications of labor or delivery									
Abnormal pelvic measurements	4 (8%)	46	50	0	1	1	4 (8%)	47	51
Abnormal presentation	2 (29%)	5	7	0	1	1	2 (25%)	6	8
Operative delivery	2 (6%)	34	36	0	4	4	2 (5%)	38	40
Premature rupture of membranes	0	8	8	0	0	0	0	8	8
Uterine inertia	0	7	7	0	0	0	0	7	7
Cephalopelvic disproportion	0	0	0	0	1	1	0	1	1
Other complications	0	4	4	0	0	0	0	4	4
Total	8 (7%)	104	112	0	7	7	8 (7%)	111	119

TABLE 10.—*The Comparative Incidence of Premature Births to Women with Acute and Chronic Disorder and Those with Normal Pregnancies—(Single Births Only)*

Condition	Live-Born			Stillborn			Live-Born and Stillborn		
	Premature	Full Term	Total	Premature	Full Term	Total	Premature	Full Term	Total
White Race—Criterion of prematurity: birth weight less than 5 pounds 8 ounces (2,500 Gm.)									
No abnormality	201 (5%)	3,805	4,006	21 (57%)	16	37	222 (5%)	3,821	4,043
Acute infections	48 (12%)	350	398	9 (64%)	5	14	57 (14%)	355	412
Chronic disorders	40 (10%)	369	409	11 (79%)	3	14	51 (12%)	372	423
Accidents	8 (8%)	87	95	1 (50%)	1	2	9 (9%)	88	97
Complications of pregnancy	6 (7%)	82	88	0	0	0	6 (7%)	82	88
Complications of labor and delivery	13 (8%)	144	157	4 (44%)	5	9	17 (10%)	149	166
Negro Race—Criterion of prematurity: birth weight less than 5 pounds 8 ounces (2,500 Gm.)									
No abnormality	244 (9%)	2,588	2,832	19 (54%)	16	35	263 (9%)	2,604	2,867
Acute infections	60 (19%)	254	314	7 (58%)	5	12	67 (21%)	259	326
Chronic disorders	39 (14%)	240	279	6 (33%)	12	18	45 (15%)	252	297
Accidents	7 (18%)	32	32	0	0	0	7 (18%)	32	39
Complications of pregnancy	4 (8%)	44	48	0	0	0	4 (8%)	44	48
Complications of labor and delivery	15 (13%)	97	112	0	7	7	15 (13%)	104	119
Negro Race—Criterion of prematurity: birth weight less than 5 pounds 3 ounces (2,350 Gm.)									
No abnormality	145 (5%)	2,687	2,832	18 (51%)	17	35	163 (6%)	2,704	2,867
Acute infections	44 (14%)	270	314	6 (50%)	6	12	50 (15%)	276	326
Chronic disorders	26 (9%)	253	279	6 (33%)	12	18	32 (11%)	265	297
Accidents	6 (15%)	33	39	0	0	0	6 (15%)	33	39
Complications of pregnancy	4 (8%)	44	48	0	0	0	4 (8%)	44	48
Complications of labor and delivery	8 (7%)	104	112	0	7	7	8 (7%)	111	119

pelvic disproportion and an abnormal presentation of the fetus, and they are so listed in the tables.

COMMENT

The majority of the maternal diseases and abnormal conditions described in this report seemed to exert a slight influence in increasing the incidence of prematurity among the newborn infants (table 10). The significance of these differences of rates has not been determined because of the paucity of numbers of patients in each subgroup. Among the total number of mothers of premature infants, acute and chronic infections occurred relatively infrequently. Of the entire series of 682 white mothers who gave birth to premature infants, 57, or 8 per cent, had acute infections and 51, or 7 per cent, had chronic disorders. Accidents and other complications occurred much less frequently. The incidence of these disorders was approximately the same among the Negro patients as among the white.

SUMMARY

Acute infections occurred in 412 white women during their pregnancies, and 57, or 14 per cent, of their offspring were premature infants. Among 326 Negro women with similar conditions, 67, or 21 per cent, gave birth to premature infants. When the standard of prematurity for the Negro infants was adjusted to include only those whose birth weight was less than 5 pounds, 3 ounces (2,350 Gm.) the rate of prematurity was 15 per cent. Although these rates were well above those of infants whose mothers had normal healthy pregnancies (5 per cent of the white offspring; 9 per cent and 6 per cent respectively of the two categories of Negro offspring), the numbers of patients were too small to permit statistical analysis.

Chronic disorders of pregnancy were associated with premature delivery in 12 per cent of the white patients and in 15 per cent and 11 per cent respectively of the Negro mothers with offspring in the two categories.

Much less frequent in occurrence were accidents and various complications of pregnancy, labor and delivery. Prematurity rates associated with these conditions were variable, ranging from 7 to 18 per cent, but the total numbers in each subgroup were extremely small.

Case Reports

ACUTE LYMPHATIC LEUKEMIA AND PREGNANCY

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THE ASSOCIATION of leukemia and pregnancy is of interest to the pediatrician for several reasons. Of primary importance is an understanding of the effect of the disease on the child during the gestational period and in the neonatal period.

According to the literature, the association of leukemia and pregnancy is a rare condition. In 1943, McGoldrick and Lapp [1] stated that there had been 79 cases of proved association reported to that date. Since 1943 there have been 5 more cases of chronic myelogenous leukemia and pregnancy described in the literature.[2]. Of these cases, 34 were cases of acute leukemia. Nine of the 34 were cases of acute lymphatic, 17 of acute myelogenous and 2 of acute hemoblastic leukemia, and the others were unclassified.

One reason for sterility in the leukemic woman is the presence of secondary amenorrhea. The genital tract may also be massively infiltrated.[2b]

Leukemia has never been shown to pass the placental barrier. Experimental studies by Burchenal,[3] who used two strains of mouse leukemia, bears out this important consideration. This investigator transmitted acute lymphatic leukemia and chronic myelogenous leukemia to separate litters of pregnant mice by giving intravenously 1 cc. of cell suspension from the spleens of leukemic mice. Eighteen of the recipients died of the disease. These 18 had 114 offspring. Of the 18 mothers, 7 died with the fetus in utero. Six died post partum; their young died because of the lack of foster parents. Five died post partum, but their young were raised by foster parents. The mothers' uteri showed massive infiltration. The leukemic cells were found only on the maternal

From the Department of Pediatrics, Permanente Foundation Hospitals, Oakland and Richmond, Calif.

1. McGoldrick, J. L., and Lapp, W. A.: Leucemia and Pregnancy, Am. J. Obst. & Gynec. **46**:711 (Nov.) 1943.

2. (*a*) Moloney, W. C.; Heffernan, R. J., and Kasdon, S. C.: Leukemia in Pregnancy, J. A. M. A. **122**:1170 (Aug. 21) 1943. (*b*) Hochman, A.: Leukaemia and Pregnancy, J. Obst. & Gynaec. Brit. Emp. **51**:231 (June) 1944. (*c*) Applebaum, H. S.: Case of Acute Leukemia Complicating Pregnancy, Ohio State M. J. **40**:536 (June) 1944. (*d*) Angelucci, H. M.: Myelogenous Leucemia Complicating Pregnancy, Am. J. Obst. & Gynec. **48**:125 (July) 1944.

3. Burchenal, J. H.: Experimental Studies on the Relation of Pregnancy to Leukemia, Am. J. Cancer **39**:309 (July) 1940.

side of the placenta, and the fetal circulation was completely normal. None of the offspring had leukemia.

That the human placenta acts as a barrier to the passage of leukemic cells has been shown. Ohlsson [4] found normal blood cells in the chorionic villi of the placenta of a leukemic woman and leukemic cells in the intervillous spaces. The reverse has been shown by Stransky [5] and Büngeler.[6] Stransky described leukemic infiltration of the skin, spleen, liver and lymph nodes of a newborn baby. This was proved at autopsy following death at the age of 3 weeks. The mother was not leukemic. Büngeler reported congenital leukemia in a 7 month stillborn fetus with myelogenous infiltration of all organs. In this case, again, the mother was not leukemic.

Among all the cases of leukemia and pregnancy reported in the literature not one of the children born of a leukemic mother was shown to have leukemia. In addition, no other congenital abnormalities have ever been ascribed to these children.

Leukemia in the mother, however, is a definite cause of premature birth of the offspring. Of 20 mothers with acute leukemia, 11 had spontaneous abortions and 9 went to term with 3 resultant stillbirths. For these 20 offspring there was a fetal mortality rate of 60 per cent. There were 9 stillborn infants, 3 neonatal deaths and 8 live babies.[1]

REPORT OF A CASE

M. B., a 26 year old white housewife, had her last menstrual period on Jan. 5, 1945. She was seen in the outpatient department for the first time on March 30, with the complaint of nausea for three weeks and backache and cramps for one week. Physical examination revealed only a uterus enlarged to the size of the organ at two and a half months of pregnancy.

Laboratory work on this date revealed the following data. A complete blood count showed: 77 per cent hemoglobin, 4,510,000 red cells and 5,800 white cells per cubic millimeter, with 65 per cent neutrophils, 27 per cent lymphocytes, 6 per cent monocytes and 1 per cent basophils. (No abnormal cells were noted on the smear.) The blood type was IV (O), and it was positive for the Rh factor. The Kline test elicited a negative reaction. Cultured material from the cervix uteri was sterile.

From March 30 to August 9 the patient was followed in the prenatal clinic. Her course seemed normal. She stated that she had felt better during this pregnancy than during either of her two previous pregnancies. There had been no fatigue, and there was a steady gain in weight.

On August 9 she was admitted to the hospital with the complaint that for two weeks previously her gums had bled spontaneously. Twenty-four hours

4. Ohlsson, I.: Ein Fall von Leukämie und Schwangerschaft, Acta gynec. Scandinav. **3**:317, 1924-1925.

5. Stransky, E.: Bemerkungen zur Arbeit "Angeborene Leukämie," Frankfurt. Ztschr. f. Path. **43**:173, 1932.

6. Büngeler, W.: Angeborene Leukämie, Frankfurt. Ztschr. f. Path. **41**:257, 1931.

before entry a frontal headache and fever had developed. Physical examination revealed a well nourished, well developed young woman, who was in no distress. Small, hard. nontender, discrete, movable anterior and posterior cervical, axillary and inguinal lymph nodes were palpated. A small blood clot was observed in the left nostril. The liver was firm, nontender and palpable 3 fingerbreadths below the right costal margin. The spleen was firm, nontender and palpable 2 fingerbreadths below the left costal margin. The fundus of the uterus was palpable 1 fingerbreadth above the level of the umbilicus.

Laboratory studies on that date revealed the following data. A complete blood count showed: —75 per cent hemoglobin, 4,160,000 red cells per cubic millimeter, a color index of 0.9 and 170,000 white cells per cubic millimeter with 5 per cent neutrophils, 95 per cent lymphocytes and 2 per cent stab cells. Nucleated erythrocytes were noted on the smear. The platelet count was 314,000 per cubic millimeter. The reticulocyte count was less than 0.1 per cent. The hematocrit reading was 33 volumes per cent of red cells (packed) and 5 volumes per cent of white cells (packed). The bleeding time was three minutes, and the clotting time was two minutes. Clot retraction began at one hour and forty-five minutes and was complete at four hours and forty-five minutes. The prothrombin time was 100 per cent of normal. Determinations of blood chemistry showed 4.4 Gm. of albumin and 3 Gm. of globulin per hundred cubic centimeters. Sternal puncture revealed extreme hyperplasia due to increased numbers of lymphocytes, of which one third were blast cells. All other marrow elements were greatly decreased.

Her progress in the hospital was uneventful save for a swinging temperature curve reaching 101 F. at 4 p. m. each day. She was discharged on August 15.

The patient reentered the hospital on August 22. The history of the interval revealed that she had had fever, malaise, weakness and bleeding from the gums. The day before entry she had had several bouts of hematemesis of bright red blood and had gradually become lethargic and unresponsive. Physical examination at this time revealed a semicomatose, pale young woman who responded slowly to questions. Her blood pressure was 108 mm. of mercury systolic and 70 mm. of mercury diastolic. The pulse rate was 96 beats per minute and the respiration rate was 24 per minute. Blood was noted on her lips and buccal mucosa. Her gingiva were hyperplastic. Numerous small petechiae were present over the body and extremities. Examination of the heart showed a moderate systolic murmur, loudest at the pulmonary area. The edge of the liver was down 5 fingerbreadths below the right costal margin. The spleen was palpable 2 fingerbreadths below the left costal margin. The fundus of the uterus was palpated 2 fingerbreadths above the umbilicus. The fetal heart rate was 130 per minute.

Laboratory studies on this last admission revealed the following data. A complete blood count showed: 52 per cent hemoglobin, 2,510,000 red blood cells per cubic millimeter, a color index of 1 and 419,500 white blood cells per cubic millimeter, with 2 per cent neutrophils and 98 per cent lymphocytes. Urinalysis showed albumin (4 plus), and sediment loaded with red blood cells. Testing of the clot revealed no clot retraction. The bleeding time was two minutes. The clotting time was six minutes. The platelet count was 36,000 per cubic millimeter. The reticulocyte count was less than 0.3 per cent. The hematocrit reading was 20 per cent packed cell volume. Prothrombin time was 100 per cent of normal. Chemical examination of the blood showed 3.9 Gm. of albumin and 3.1 Gm. of globulin per hundred cubic centimeters. Sternal marrow revealed hyperplasia consisting almost entirely of lymphoblasts. Only a few granulocytes were seen.

In spite of two transfusions, she failed rapidly and died nineteen and a half hours after her final entry into the hospital.

Postmortem examination confirmed the clinical diagnosis. There was massive leukemic infiltration of the adrenal glands, liver, pancreas, spleen, kidneys, lungs and heart. The uterus contained a 7 month dead fetus, which had congenital clubfeet and spina bifida.

A recapitulation of some of the laboratory data is given in the table.

Laboratory Observations

Factors	3/30/45	8/9/45	8/22/45
Complete blood count			
Hemoglobin	77%	75%	52%
Red cell count	4,510,000/cu. mm.	4,110,000/cu. mm.	2,510,000/cu. mm.
Color index	0.86	0.9	1.0
White cell count	5,800/cu. mm.	170,000/cu. mm.	419,000/cu. mm.
Neutrophils	65%	5%	2%
Lymphocytes	27%	95%	98%
Monocytes	6%	0	0
Eosinophils	1%	0	0
Basophils	1%	0	0
Stab cells	3%	2%	0
Others	0	Nucleated erythrocytes	0
Platelet count	—	314,000/cu. mm.	36,000/cu. mm.
Reticulocyte count	—	Less than 0.1%	Less than 0.3%
Bleeding time	—	3 min.	2 min.
Clotting time	—	2 min.	6 min.
Prothrombin time	—	100%	100%
Clot retraction			
Began in	—	1 hr. 45 min.	No retraction
Complete in	—	4 hr. 45 min.	No retraction
Hematocrit			
Erythrocytes	—	33 vol., %	—
Buffy layer	—	5 vol., %	—
Total	—	38 vol., %	—

COMMENT

This is the tenth reported case of acute lymphatic leukemia and pregnancy. From the point of view of the pediatrician this case is important because of the observation of congenital deformities in the offspring. However, a causal relationship is extremely doubtful because of the time elements involved. In textbooks on developmental anatomy spina bifida is stated to develop about the fourth week and clubfeet about the twelfth week of fetal life.[7] In this patient no signs or symptoms of leukemia were observed until the seventh month of her gestational period.

The consensus of the literature is that intensive and radical therapeutic measures may be instituted with no great danger to the baby. McGoldrick and Lapp [1] have recommended the use of solution of potassium arsenite U. S. P. Moloney,[2a] Hochman [2b] and Angelucci [2d] all used high voltage roentgen ray therapy on the leukemic mother without harming the offspring. However, when in spite of therapy the leukemic mother fails rapidly, immediate cesarean section is probably

7. Arey, L. B.: Developmental Anatomy, ed. 4, Philadelphia, W. B. Saunders Company, 1942, pp. 148-149.

indicated. If section is delayed, the baby may die in utero because of inanition of the mother.

SUMMARY

Acute lymphatic leukemia associated with pregnancy is a rare condition. This paper presents the tenth reported instance in the medical literature. In this case the infant presented congenital deformities. However, we feel that the leukemia of the mother was not responsible for the presence of the congenital clubfeet or the spina bifida, because of the discrepancies in the time factors involved.

In no reported instance have both the mother and the baby had leukemia. The placenta acts as a barrier and prevents transmission of leukemic cells to and from the offspring.

The fetal mortality rate and the prematurity rate are extremely high when the mother has leukemia. This is probably due to inanition of the mother.

The use of solution of potassium arsenite U. S. P. and strong solution of iodine U. S. P. and high voltage roentgen ray therapy is probably indicated in this condition, since no adverse affects on the offspring have ever been noted and since the mother's course may probably be eased and prolonged.

If the leukemic mother is failing rapidly, immediate cesarean section is probably indicated. If section is delayed, the baby may die in utero because of inanition of the mother.

SPONTANEOUS PNEUMOTHORAX IN THE NEWBORN

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SPONTANEOUS pneumothorax in the newborn infant is relatively rare. Davis and Stevens[1] (1930) reported finding 6 instances of spontaneous pneumothorax in newborn infants among 702 consecutive roentgenographic examinations. De Costa[2] (1940) reviewed 67 reported instances of pneumothorax during the first few months of life. Ten days was set as the maximum time for the recognition of pneumothorax associated with birth. In this study he considered 46 cases in which pneumothorax occurred in direct connection with birth plus 2 of his own. He suggested the classification "spontaneous pneumothorax abrupta" for those cases in which symptoms are noted from birth or shortly thereafter, and "pneumothorax lenta," for those in which there are mild symptoms with gradual onset. In the addendum 3 additional unreported cases were commented on. In this series of 72 cases a cesarean section was performed only four times (Emmert[3] [1930], Bertin[4] [1936], Holz[5] [1936] and Rothman[6] [1937]).

Silver[7] (1939) reported a case and recommended that the term spontaneous pneumothorax in the newborn be limited to the first four or five days of life and that lesions that make their first appearance after this time be considered as disturbances having a separate cause. Elkin[8] (1941) presented 3 additional cases of spontaneous pneumothorax in the newborn and mentioned 3 other cases, not previously reviewed, 2 reported by Donahoe[9] and 1 by Leopold and Castrovinci.[10]

From the Department of Pediatrics, University of Louisville School of Medicine, Louisville, Ky., services of Dr. James W. Bruce and Dr. W. W. Nicholson.

1. Davis, C. H., and Stevens, G. W.: Value of Routine Radiographic Examinations of the Newborn Based on a Study of 702 Consecutive Cases, Am. J. Obst. & Gynec. **20**:73-76, 1930.

2. De Costa, E. J.: Spontaneous Pneumothorax of the Newborn, Am. J. Obst. & Gynec. **39**:578-592, 1940.

3. Emmert, F.: The Danger of Mouth-to-Mouth Breathing in Resuscitation of the New Born Infant, Am. J. Dis. Child. **39**:1268-1269 (June) 1930.

4. Bertin, E. J.: Pneumothorax in the Newborn, Radiology **27**:584-593, 1936.

5. Holz, I.: Beitrage zur Frage des Spontanpneumothorax bei Neugeborenen, Kinderärztl. Praxis **7**:3-9, 1936.

6. Rothman, P. E.: Spontaneous Pneumothorax of Newly-Born, Arch. Dis. Childhood **12**:119-122, 1937.

7. Silver, H. B.: Spontaneous Pneumothorax in the Newborn, Am. J. Dis. Child. **57**:907-915 (April) 1939.

8. Elkin, W. P.: Neonatal Pneumothorax, South. M. J. **34**:929-933, 1941.

9. Donahoe, W. E.: Pneumothorax in Newborn Infant, Journal-Lancet **52**: 699-701, 1932.

10. Leopold, J. S., and Castrovinci, F.: Traumatic Pneumothorax in the Newborn, J. Pediat. **9**:620-623, 1936.

In 1943 Salmon and Forbes[11] reported 3 cases and later the same year Johnson[12] reported the case of an infant delivered by cesarean section in whom spontaneous pneumothorax developed on the second day of life, with recovery.

It is the purpose of this communication to report a case of spontaneous pneumothorax with recovery, occurring in a 5 day old infant delivered by cesarean section.

REPORT OF A CASE

A white girl was delivered at the Louisville General Hospital at 11:46 a. m., Nov. 24, 1944, by cesarean section, with the mother under spinal anesthesia. The indication for section was placentae ablatio. Except for 3 breech deliveries and 1 transverse presentation in which delivery was by version and breech extraction, the previous obstetric history of the mother was noncontributory. At delivery the infant was cyanotic and had a weak cry, but the respirations were normal. Resuscitation consisted of bulb suction and cutaneous stimulation. The findings on physical examination were entirely normal. The birth weight was 7 pounds 7½ ounces (3,375 Gm.).

After the usual starvation period of twelve hours, she was given breast feedings supplemented with 5 per cent dextrose in water.

On the fifth day, Nov. 29, 1944, at 8:00 a. m. she was found to have an unexplained fever, with the temperature 103.6 F. As the weight had now dropped to 6 pounds and 4 ounces (2,835 Gm.) and dehydration was evident, breast feedings were discontinued, and a 45 cc. formula consisting of evaporated milk, water and 5 per cent carbohydrate was substituted. At 7:00 p. m. the temperature was 100.6 F. The infant was cyanotic, dehydrated, lethargic and flaccid and displayed a mild convulsion. Treatment consisted of the supplying of oxygen, feedings by gavage, administration of phenobarbital ¼ grain (0.015 Gm.) and of sulfadiazine 0.125 Gm. every four hours and 100 cc. of 2.5 per cent dextrose solution given subcutaneously. The white blood cell count was 17,000 per cubic millimeter, with 54 per cent polymorphonuclear leukocytes and 46 per cent lymphocytes. A roentgenogram of the chest was taken but unfortunately was not seen until the following day (fig. *A*). On November 30, the temperature was normal and respirations were shallow, but an examination of the chest revealed nothing remarkable. A roentgenogram of the chest at this time, also revealed a right pneumothorax (see fig. *B*). Administration of sulfadiazine was then discontinued. The cyanosis gradually improved, and the administration of oxygen was discontinued on Dec. 1, 1944. On December 4, a roentgenogram of the chest (fig. *C*) revealed complete clearing of the pneumothorax. The infant was then given breast feedings again with a supplementary feeding of the formula and was discharged on December 5 with a weight of 6 pounds and 14 ounces (3,118 Gm.).

There have been two readmissions to the hospital for nonspecific diarrhea, and on both occasions the roentgenograms of the chest were entirely normal. The infant was last seen in the clinic Nov. 9, 1945, and, except for a mild nutritional disturbance, the physical examination showed nothing remarkable. Again a roentgenogram of the chest was normal.

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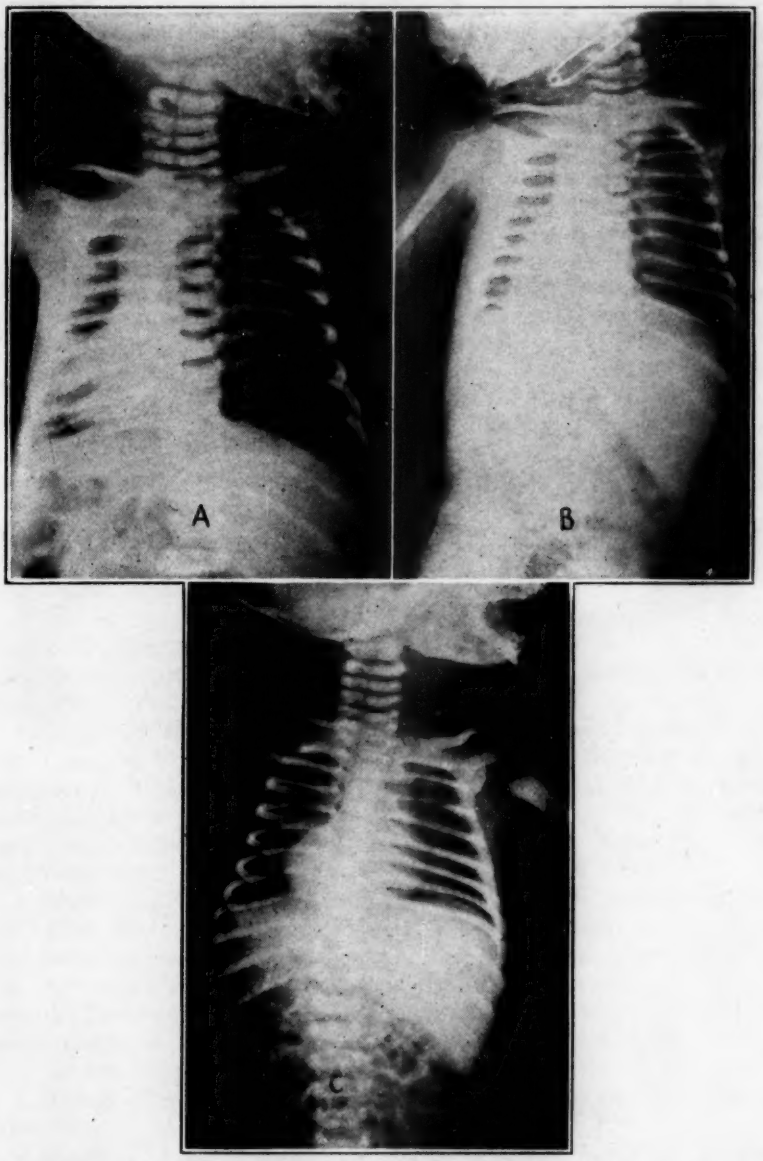
11. Salmon, G. W., and Forbes, G. B.: Pneumothorax in the Newborn Infant: Report of Three Cases, J. Pediat. **23**:50-58, 1943.

12. Johnson, G. D.: Case Report: Pneumothorax in the Newborn, J. South Carolina M. A. **39**:299-300, 1943.



Roentgenograms of the chest showing spontaneous pneumothorax: *A*, appearance of the chest on the fifth day; *B*, roentgenogram on November 30, also revealing a right pneumothorax, and *C*, appearance of the chest on December 4 revealing complete clearing of the pneumothorax.

COMMENT AND CONCLUSION

As clinical signs and symptoms of spontaneous pneumothorax in the newborn are not always prominent, the diagnosis can be made only by the use of roentgenography. It would seem from the work of Davis and Stevens [1] that spontaneous pneumothorax of the newborn is more common than a review of the medical literature would indicate.

Treatment of spontaneous pneumothorax in the newborn should be conservative, and aspiration should be reserved for the more severe forms.

Trauma during delivery probably plays a major role in the causation of spontaneous pneumothorax of the newborn, but it is interesting to note that this is the sixth case reported of an infant delivered by cesarean section.

PRIMARY TUBERCULOSIS OF THE CONJUNCTIVA

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ALTHOUGH tuberculosis of the conjunctiva is no longer commonly observed, primary tuberculosis of the conjunctiva is even more rare. Since Koester [1] first reported a case of tuberculosis of the conjunctiva in 1873, only one large series of cases of primary tuberculosis of the conjunctiva has been reported, i. e., by Blegvad [2] in 1936, who reported the cases of 40 patients with primary conjunctival tuberculosis seen at the Finsen Institute from 1909 to 1934. Samuelson [3] observed only 7 patients with tuberculosis of the conjunctiva, and 3 of these had primary infections.

In this country, the number of cases reported [4] has been even fewer than those reported from European sources.[5] Burchell [6] did not observe a single case in twenty years at the New York Eye and Ear Infirmary, where there was an average annual admission of 30,000. Only isolated cases were reported from American sources by Hansell,[7] Henderson,[8] Jackson,[9] Peter [10] and Shoemaker.[11]

From the service of Dr. Harry S. Altman, Department of Pediatrics, Lincoln Hospital, New York.

1. Koester, quoted by Eyre.[5]

2. Blegvad, D.: Fortgesetze Untersuchungen über die conjunctivale Tuberkulose, Acta ophth. **14**:200, 1936.

3. Samuelson, D.: Primary Tuberculosis of Conjunctiva, Arch. Ophth. **15**:975 (June) 1936.

4. Coover, D. H.: Tuberculosis of the Conjunctiva, Am. J. Ophth. **3**:206, 1920. Cohen, M.: Tuberculosis of the Conjunctiva, Arch. Ophth. **48**:96, 1919. Thompson, J.: Report of a Case of Primary Tuberculosis of the Conjunctiva, Ann. Ophth. **15**:76, 1906. McKenzie, W. H.: Tuberculosis of the Conjunctiva, Am. J. Ophth. **22**:744, 1939. Bordley, J.: Tuberculosis of the Conjunctiva, Ophth. Rec. **11**:368, 1902.

5. Sattler, H.: Tubercular Ulceration of the Conjunctiva, Irish Hosp. Gaz. **2**:101, 1874. Eyre, J. W. H.: Tuberculosis of the Conjunctiva, Lancet **1**:1319, 1912. Sergievsky, L.: Tuberculosis and the Eye, in Collected Papers Dedicated to M. Averbach, Moscow, State Publishers, 1935, p. 422. Saemisch, T.: Tuberkulose der Bindehaut, in Graefe, A., and Saemisch, T.: Handbuch der gesamten Augenheilkunde, ed. 2, Leipzig, W. Engelmann, 1909-1911, vol. 5, p. 484.

6. Burchell, cited by Sitcheveska and Sedam.[12]

7. Hansell, H. F.: A Case of Tuberculosis of the Conjunctiva, Ann. Ophth. **10**:398, 1901.

8. Henderson, F. L.: A Case of Tuberculosis of the Conjunctiva, Tr. Missouri M. A., 1903, p. 383.

9. Jackson, E.: Tuberculosis of the Conjunctiva, Ophth. Rec. **12**:417, 1903.

10. Peter, L. C.: Tuberculosis of the Conjunctiva and Sclera Following Removal of a Pigmented Papilloma of the Conjunctiva, Arch. Ophth. **41**:240, 1912.

11. Shoemaker, W. T.: A Case of Tuberculosis of the Conjunctiva, Tr. Coll. Physicians, Philadelphia **36**:304, 1914.

In 1943, Sitchevska and Sedam [12] collected reports of 4 additional cases from the American literature, to which they added their own case.

The condition usually described as a "primary complex" when one refers to the pathology of tuberculosis consists of a local lesion and associated involvement of a regional lymph node. A similar condition is found in primary tuberculosis of the conjunctiva.[13] The diagnosis of primary infection of the conjunctiva usually is based on a number of premises: (1) that there is no other demonstrable lesion elsewhere in the body as far as can be determined; (2) that the process is unilateral, and (3) that there is involvement of the satellite and preauricular nodes and other regional nodes.

The method of infection also has been the topic of much discussion. Duke-Elder [14] cited experimental cases of hematogenous infection and of infection produced by local inoculation in animals. It seems, however, that in animals which already have tuberculosis elsewhere, conjunctival implantation of tubercle bacilli did not always lead to infection of the conjunctiva and the regional lymph nodes.[15] In general, the methods of inoculation of tuberculosis on the conjunctiva are considered to be.

1. Primary infection—exogenous, by definition
2. Secondary infection
   (*a*) Exogenous (as by a finger touching the eye)
   (*b*) Endogenous (as by the blood stream)
   (*c*) By direct extension (as in lupus or from tuberculosis of the orbit)

It is interesting that it has been postulated [14] that primary tuberculosis of the conjunctiva occurs in children and adults early, before the allergic state to the organism has set in. This is analogous to the onset of primary complexes anywhere in the body. Probably this explains why primary tuberculous conjunctivitis usually occurs before the age of 30. Sattler [16] in 1891 listed four classic types of tuberculous lesions of the conjunctiva, and Lafon [16] in 1908 added a fifth:

1. The ulcerative type
2. The nodular type
3. The hypertrophic papillary type
4. The polypoid type
5. The conjunctival tuberculoma type

All five of these types are based on the pathologic changes of tuberculous lesions in general and are either ulcerative or hyperplastic.

The case to be presented is an additional one for the literature, and is, we believe, one of primary tuberculosis of the conjunctiva of the ulcerative type.

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12. Sitchevska, O., and Sedam, M.: Primary Tuberculosis of the Conjunctiva, Arch. Ophth. **30**:196 (Aug.) 1943.

13. Fuchs, E.: Textbook of Ophthalmology, ed. 8, Philadelphia, J. B. Lippincott Company, 1924, p. 495.

14. Duke-Elder, W. S.: Textbook of Ophthalmology, St. Louis, C. V. Mosby Company, 1938, vol. 2, p. 1630.

15. Lagrange, N.: Innoculation de la tuberculose et superinfection experimentale par la voie conjunctivale, Ann. d'ocul. **160**:849, 1923. Parinaud, H.: Tuberculose primitive de la conjunctive: Valeur des inoculations expérimentales pratiqués dans la chambre antérieure de l'oeil, Gaz. hebd. de méd. **21**:398, 184.

16. Cited by Duke-Elder.[14]

REPORT OF A CASE

History.—The patient was admitted to the hospital on April 16, 1945. He was a 10 year old white boy with a history of a "lump" in front of the right ear for one week. About one week before admission, a small mass was noted in front of the right ear, which grew larger each day.

Two days after the onset, another lump was noted beneath the right jaw, and this was associated with pain on opening the mouth. Two days later, a swelling was noted in the right eye, and the patient was brought to the outpatient department, where cold compresses were prescribed; because of the rapid progress of the condition, the patient was admitted to the ward. The past history of the patient and the family history were noncontributory. There was no history of exposure to tuberculosis.

Diagnosis.—At admission the diagnosis was blepharitis with adenopathy.

Fig. 1.—Ulcerative lesion of primary tuberculosis of the conjunctiva.

Physical Examination.—Examination revealed a well developed, well nourished 10 year old white boy with an obvious right-sided periorbital edema. The temperature was 100.6 F. The patient's right upper eyelid was edematous. On the conjunctival surface of the right lower lid there was noticeable injection, most severe on the peripheral rim of the conjunctival sac. There was an area of ulceration of about 1 to 2 mm. in the lateral corner of the lower right conjunctival sac, with whitish spots about it about 1 mm. in diameter.

In front of the right ear and extending underneath the right angle of the jaw, there was a mass about 1 inch (2.5 cm.) in diameter, which was hard and tender to palpation. Examination of the throat revealed tonsils which were moderately injected and hypertrophied. The patient also had eight umbilicated papular lesions of the groin, which were later diagnosed as molluscum contagiosum.

Laboratory Data.—The urine was repeatedly normal. White blood cells numbered 10,300 per cubic millimeter. The hemoglobin content was 14.6 Gm. per hundred cubic centimeters. The Mantoux test (1 to 10,000 dilution of old tuberculin) elicited a positive (3 plus) reaction. Roentgenologic examination of the chest and abdominal regions revealed no abnormality. The Wassermann reaction was negative.

Course.—The patient was treated with sulfadiazine 2 Gm. initially and 1 Gm. every four hours. Other therapy consisted of administration of cod liver oil and ferrous sulfate, irrigation of the eye with boric acid U. S. P. and cold compresses on the neck and right preauricular area. A 5 per cent sulfathiazole ointment was applied to the eye twice a day following irrigation. Blood was cultured but failed to reveal

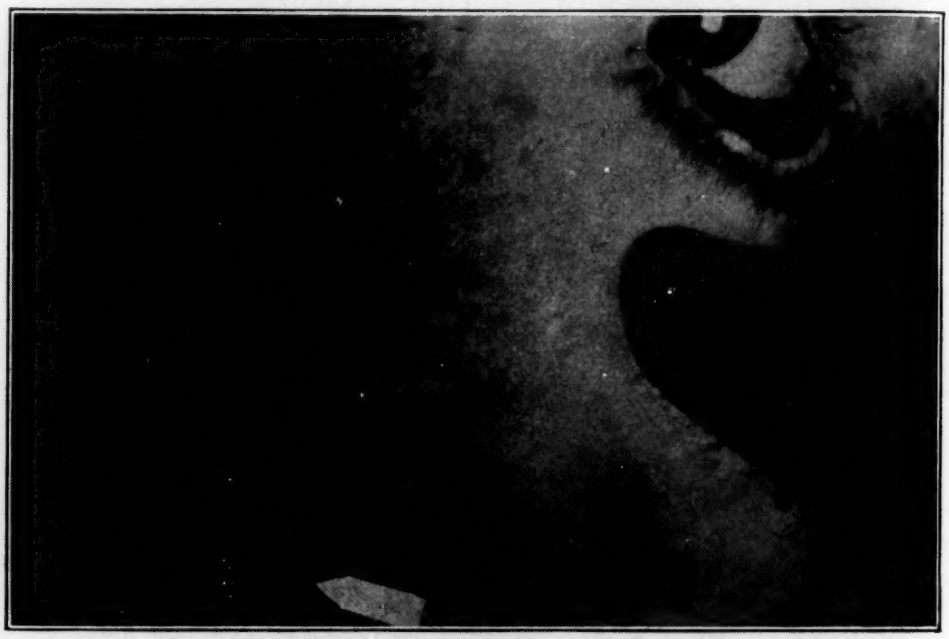

Fig. 2.—A photograph showing (arrow) the swelling on the side of the face denoting satellite adenopathy.

the organism. In one week, the swelling of the glands began to subside, but the eye remained as it was on the patient's admission.

On April 23, the patient was seen by a member of the department of ophthalmology, who described the lesion as "a well demarcated, membranous-appearing, dirty gray ulcer of the right lower lid—granulomatous in nature." Biopsy of the ulcerated area on April 26 was described by the pathologist as revealing "granulation tissue containing typical tubercles with the Langhans type of giant cells." Special stains revealed the presence of acid-fast bacilli. Material scraped from the conjunctival ulcer on April 26 and cultured on Petragrani medium produced a growth of acid-fast bacilli.

The temperature curve ran to about 100 F., with evening rises to about 100.6 F. irregularly throughout the hospital stay. The patient was finally transferred to another hospital for special treatment.

SUMMARY

Primary tuberculosis of the conjunctiva, the method of infection, the diagnosis and the classification are described briefly.

This condition is rare, and it usually occurs early in life.

It may occur by means of exogenous infection only; when it so occurs, it is unilateral and has associated infected satellite lymph nodes.

The pathologic changes may be ulcerative or may be of any one of the hyperplastic types.

A case of primary tuberculosis of the conjunctiva in a 10 year old child is presented in which the diagnosis was made by biopsy and culture from scrapings of the lesion and in which no other site of tuberculosis was found except the conjunctiva and its satellite lymph gland.

Assistance in the study of this case was given by Dr. Harry S. Altman and the staff of the Department of Pediatrics, Dr. Castroviejo and Dr. Di Carlo of the ophthalmology staff of Lincoln Hospital and Dr. J. George Sharnoff, pathologist. The photography was done by Dr. Boardman.

Abstracts from Current Literature

Hygiene; Growth and Nutrition; Public Health

ENDURANCE OF YOUNG MEN: ANALYSIS OF ENDURANCE EXERCISES AND METHODS OF EVALUATING PHYSICAL FITNESS. THOMAS KIRK CURETON and others, Monographs of the Society for Research in Child Development, 1945, vol. 10, no. 1.

The National Research Council, through the Society for Research in Child Development, has published a three hundred page research report on "Endurance of Young Men." The report represents a two year study made by five members of the faculty of the University of Illinois School of Physical Education. The study was planned and directed by Professor Thomas K. Cureton, assisted by Warren J. Huffman, Lyle Welser, Ramon Kireilis and Darrel Latham. Data were collected in the University of Illinois service classes and also in the Urbana High School. Some 3,000 men were tested with twenty-eight endurance exercises and also a portion of these were tested with the best known organic condition tests.

In analyzing these twenty-eight exercises, the problem has been to show how reliably they can be controlled in physical education testing, to show how they interrelate and to prove the value of each exercise in the prediction of all-around ability.

The report includes more than two thousand correlations and much advanced statistical work for predicting performance and for analyzing fundamental constituents of muscular and organic endurance. The factor analysis work in the report shows that there were four principle factors in the kind of endurance tested in physical education. Three of these aspects of endurance have to do with the principal neuromuscular pattern combining: (1) lateral muscles, (2) limb locomotive muscles and (3) arm extensor muscles. In addition, organic endurance shows up as a dominant factor in endurance running, and this same factor is not well indicated in the three types previously mentioned. This shows that in order to measure all-around endurance of an athletic type, all four of these constituent factors must be measured.

The report presents new equations for predicting all-around endurance or any one of the four types of endurance mentioned. Several tests are given in the back of the report which are of considerable practical value to physical education departments, although the principal contribution of the report is to fundamental knowledge about endurance and about the tests which measure it. Never before have men been tested so extensively in so many endurance events, and this is the first publication which reports performances of men and boys in endurance events such as the 4 mile steeple chase, the 2 mile run and mile run and the 1,000 yard drop-off run. The report shows that the step test devised by the Harvard Fatigue Laboratory research workers is very poor for measuring all-around athletic endurance of the type included compared with the other possible combinations of test items. It also shows that the Army and the Navy have used some very fine events in their testing programs, such as chinning the bar, push-ups, and the 300 yard shuttle run. However, the mile run is shown to be of greatest all-around value in measuring all of the constituents of endurance. The lateral exercises such as raising the right leg to the side and the left leg are shown to be of great all-around value in predicting muscular endurance. These items are better than some in the Army and Navy tests which are now in use, according to the findings in this research.

The study is a cooperative publication, partly financed by the Research Board of the University of Illinois and published by the National Research Council in

Washington. Testing facilities in the new physical fitness laboratory of the University of Illinois were used in making the organic tests. This laboratory is well equipped for measuring various aspects of physical fitness of the human body as exhibited through test exercises.

Newborn

HEMOLYTIC ANEMIA OF THE NEWBORN (ERYTHROBLASTOSIS FETALIS). RUTH G. ALEMAN, New Orleans M. & S. J. **98**:278 (Dec.) 1945.

Three cases of erythroblastosis fetalis are reported, 2 of severe illness and 1 of mild. All 3 patients survived under treatment consisting of transfusions with Rh negative blood, vitamin K, vitamin C and oxygen.

BERKLEY, Beverly Hills, Calif.

Acute Contagious Diseases

PERTUSSIS IMMUNIZATION PROGRAM OF THE BOSTON HEALTH DEPARTMENT: THE COMPARATIVE VALUE OF TWO DIFFERENT ANTIGENS. LEO CRAVITZ and JOHN H. CAULEY, J. A. M. A. **129**:539 (Oct. 20) 1945.

A study was made of 3,006 children immunized against pertussis by the Boston Health Department in 1942 and 1943. Sauer's vaccine (Parke, Davis) in doses of 1, 2 and 3 cc. at intervals of three weeks was given to 1,871 children. Detoxified Pertussis Antigen (Lederle) in doses of 2 cc. every three weeks for three doses was given to 1,135 children. The average age at immunization was 7.6 months.

Six cases of pertussis developed in the group immunized with Sauer's vaccine, representing a total of 1,622 person years of experience, or a rate of 3.7 annual cases per thousand. Thirty-four cases of pertussis developed in the group immunized with the Lederle antigen, representing a total of 1,153 person years of experience, or a rate of 29.5 annual cases per thousand. In 65.6 per cent of the cases of pertussis developing in the immunized group the effects were mild or very mild.

In the group immunized with Sauer's vaccine 65 exposures resulted in the 6 cases of pertussis. In the group immunized with the antigen 59 exposures resulted in the 34 cases. In the control group composed of nonimmunized siblings there were 360 exposures resulting in 298 cases. The percentage of children having the disease after exposure was therefore 9.2, 67.6 and 82.8 respectively in the three groups.

The Sauer vaccine gives excellent protection for at least the period of this study (one to two years). Detoxified Pertussis Antigen is less effective prophylactically but does modify the clinical disease.

BAIRD, Wauwatosa, Wis.

TONSILLECTOMY AND POLIOMYELITIS. W. J. MCCORMICK, Union méd. du Canada **72**:296 (March) 1943.

Tonsillectomy has an undoubted role in the etiology of poliomyelitis. Generalized lymphoid hyperplasia is associated with poliomyelitis. Vitamin B deficiency is accompanied by generalized lymphoid hyperplasia. Degenerative disease of the nervous system is accompanied by a lymphocytic reaction in the cerebrospinal fluid. In the Toronto epidemic of 1937 60 per cent of the cases of poliomyelitis following tonsillectomy were in families on relief, who constituted less than 8 per cent of the total population of the city. Any general anesthesia produces more or less anoxemia.

From these facts culled from the literature, McCormick strengthens his theory of the importance of lack of vitamin B in the production of clinical poliomyelitis.

DAFFINEE, Melrose, Mass.

COMBINED IMMUNIZATIONS. G. RAMON, Presse méd. **53**:93 (Feb. 24) 1945.

Ramon points out the value of combined immunization, and urges use of the diphtheria-tetanus-typhoid mixture. Its use in the French army has practically eliminated the outbreaks of those diseases, which were formerly problems in Army medicine. He deplores the ineffective enforcement of the law of 1938 providing for the immunization of the civilian population and asserts that in the turmoil of war and displacement such immunization would have prevented epidemics and loss of life.

DAFFINEE, Melrose, Mass.

RAPID DIAGNOSIS OF DIPHTHERIA. M. LISBONNE and H. GALERNE, Presse méd. **53**:130 (March 17) 1945.

The authors draw attention to the worth of the Manzullo technic for the rapid (three hour) growth of the diphtheria bacillus. The medium consists of 15 cc. of broth, 1.5 cc. of defibrinated blood and 1.5 cc. of a 2 per cent solution of potassium tellurite.

DAFFINEE, Melrose, Mass.

MENINGOENCEPHALITIS AFTER RUBEOLA. E. F. J. H. FALGER, Nederl. tijdschr. v. geneesk. **87**:109 (Jan. 16) 1943.

A fatal case of meningoencephalitis after measles in a woman of 26 is described. The neurologic complications after measles generally have an acute beginning. Practically without exception lymphocytes are present in the cerebrospinal fluid, which remains sterile. The anatomic changes in the central nervous system probably are caused by an anaphylactic reaction to the measles allergen.

VAN CREVELD, Amsterdam, Netherlands.

PROGNOSIS OF DIPHTHERIA IN CONNECTION WITH THE TYPE OF BACTERIUM. A. P. VAN DER WEY, Nederl. tijdschr. v. geneesk. **87**:203 (Jan. 30) 1943.

The malignant forms of diphtheria are more often caused by the gravis type than by the mitis type: the mitis type is more laryngotropic than is the gravis. The intermedius type seems to resemble the gravis more than the mitis type.

VAN CREVELD, Amsterdam, Netherlands.

THE TREATMENT OF ACUTE POLIOMYELITIS IN THE THIRD STAGE OF THE DISEASE. E. H. LA CHAPELLE, Nederl. tijdschr. v. geneesk. **88**:485 (May 20-27) 1944.

The third stage of poliomyelitis is called the stage of reparation or regression because in this stage the action of the muscles partly or totally reappears. Until far into this third stage pain on pressure and on movement is observed; therefore the disease in this stage is sometimes called the neuritic form. However, the author is of the opinion that the pains are probably caused by the irritated membranes of the brain. Careful nourishment, rest and especially heat (hot baths) have a favorable influence on these pains and on their consequences. More supporting than redressing bandages are indicated here. The author gives some indications for the method of treatment in this third stage. To stimulate the muscular activity the author especially recommends active and passive exercises in a hot bath. Faradising of the muscles is rejected, whereas galvanizing under special conditions sometimes still may prove successful.

VAN CREVELD, Amsterdam, Netherlands.

VALUE OF ACTIVE IMMUNIZATION AGAINST DIPHTHERIA. C. R. ZYERVELD, Nederl. tijdschr. v. geneesk. **88**:516 (June 3-10) 1944.

In a district near Haarlem (Netherlands) since 1939 about 75 per cent of the school children and 90 per cent of kindergarten children have been actively immu-

nized against diphtheria by means of anatoxin. In 1942 there occurred 159 cases of diphtheria, and in 1943 there were 302 cases. In 132 of the total of 461 cases the children had been immunized, and there was 1 death, and in the 329 cases in which the children had not been immunized there were 18 deaths.

VAN CREVELD, Amsterdam, Netherlands.

Acute Infectious Diseases

TREATMENT OF TETANUS WITH SERUM AND TOXOID SIMULTANEOUSLY. G. RAMON and R. RICHOU, Presse méd. **53**:277 (June 2) 1945.

Since 1937 various applications of the combined use of serum and toxoid have been set forth. The rapid elimination of serum causes a lack of protection in a subject who still has viable spores in his wound area. This protection can be built up to a higher and more permanent level by use of toxoid. With this method of treatment repeated doses of intravenous serum should no longer be necessary.

The authors suggest the following routine treatment (for adults):

As early as possible, a dose of 200,000 units of antitetanic serum is given, half intramuscularly and half subcutaneously. At that time, with a different syringe, an injection of 2 cc. of tetanus toxoid (fluid) is given. Three further injections of toxoid are given at intervals of four or five days, in dosages of 2 cc., 4 cc. and 6 cc.

DAFFINEE, Melrose, Mass.

AN EXCEPTIONAL CASE OF OXYURIASIS OF THE INTESTINAL WALL. J. BYLMER, Nederl. tijdschr. v. geneesk. **88**:24 (Jan. 1-8) 1944.

A man of 46 died with symptoms of progressive uremia after having had a severe diarrhea. At necropsy an extensive gangrenous ulceration was found in the lowest part of the rectum. In the cecum and colon there were also many small ulcers, and there were some in the ileum. Histologically gangrenous ulcers were found with numerous worms (Enterobius vermicularis [S. oxyuris]) in the submucosa and the subserosa. From the colon and the rectum a large number of small pieces were studied further, which were taken from places containing ulcers as well as from parts with a normal aspect. The number of worms present in the intestinal wall, especially in the submucosa, was excessively large; they were not all full grown, especially not the females.

The question is to what degree the Oxyuris caused the gangrenous ulcers or whether the Oxyuris invaded the intestinal wall during life or after death. That the worms were for the greater part not full grown is probably caused by the fact that the full grown females had been carried away by the diarrhea, whereas the young worms had invaded the intestinal wall via the ulcers.

VAN CREVELD, Amsterdam, Netherlands.

OBSERVATIONS ON CARRIERS OF PLASMODIUM VIVAX. F. J. A. PAESI, Nederl. tijdschr. v. geneesk. **88**:679 (July 15-22) 1944.

From the investigations of Swellengrebel it is known that in the Netherlands in the spreading of tertian malaria "healthy" carriers of Plasmodium vivax, e. g., persons who have the organisms in their body but who are practically without complaints, play an important role. The author made a study of the number and kind of the organisms in the blood of these persons and of their condition of health. For this research work he chose a quarter in the northern part of Amsterdam where in 1939 many cases of malaria were observed. Each time the number of organisms in 6,000 leukocytes was counted and their forms determined. In the Indian summer of 1940 a number of carriers of P. vivax were traced who for the most part had suffered from their first attack of malaria that summer. The blood

of these persons, all children, was studied at intervals during a long period. In 9 of the 15 children the well known variations in the number of Plasmodium organisms in the blood of malaria patients occurred with a certain regularity. The "positive phase" (increase of the number of parasites in the blood) lasted mostly ten to sixteen days, the "negative phase" (decrease of the number of parasites to zero) eight to fourteen days. Among the 6 exceptions were 5 children who in a recent stage had already lost their parasites and 1 boy without a spleen in whom the parasites always were present. Whereas the other carriers usually became free of the organisms within one year, this boy after three and one-half years still was a carrier. The new observations about the regular return of parasites have consequences for epidemiologic investigations of P. vivax carriers; after one examination without discovery of the parasites ("negative phase") a second examination is necessary only ten to sixteen days later. As regards the aspect of the parasites and their cycle of development no change in the relation of the different forms of the parasites could be found. As regards the condition of health of the carriers of P. vivax, complaints usually were absent, and the physician was called only when the number of parasites (in 6,000 leukocytes) varied between 6,000 and 24,000.

VAN CREVELD. Amsterdam, Netherlands.

Chronic Infectious Diseases

POLYNEURITIS IN TUBERCULOSIS. G. P. BAUER, Nederl. tijdschr. v. geneesk. **86:** 3274 (Dec. 26) 1942.

The author discusses 2 cases of polyneuritis in the course of active tuberculosis and tries to examine how far the tuberculosis should be regarded as a causal factor in the nervous disturbances. By references to medical literature and by an analysis of the second case it is shown that polyneuritis can be caused by avitaminosis resulting from secondary tuberculosis of the intestines. The first case belongs to a group of cases in which it is not clear whether the combination of the two conditions is accidental, or whether the tuberculosis should be regarded as a predisposing factor for the nervous disturbance.

VAN CREVELD, Amsterdam, Netherlands.

EXAMINATION OF TISSUE SECTIONS FOR TUBERCLE BACILLI BY MEANS OF THE FLUORESCENCE-MICROSCOPE. J. H. BEKKER and H. H. VINK, Nederl. tijdschr. v. geneesk. **87:**10 (Jan. 2) 1943.

The authors describe and discuss the examination of tissue sections for tubercle bacilli by means of the fluorescence microscope. The use of fluorescence-microscopy is to be preferred to examination by means of the Ziehl-Neelsen method of staining, as the color technic is simpler, the contrast stronger and the number of bacilli found greater, and the method takes less time.

VAN CREVELD, Amsterdam, Netherlands.

TUBERCULOSIS OF THE LUNG AND KIDNEY STONES. J. C. GERRITS, Nederl. tijdschr. v. geneesk. **88:**765 (Aug. 12-19) 1944.

An abnormal excretion of oxalic acid with the urine does not always give rise to the formation of renal stones. In patients suffering from tuberculosis of the lungs the author, in agreement with others, always found an abnormally high excretion of oxalic acid. No relation was found between the excretion of oxalic acid and the severity and extension of the pulmonary tuberculosis. The combination of oxalate stones and pulmonary tuberculosis is not to be found in literature. No explanation can be given for the high excretion of oxalic acid in this disease. The fact that no renal stones develop in pulmonary tuberculosis can probably be explained by an increase of the colloidal as well as of the crystalloid (oxalic acid) substances in the urine.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of Blood, Heart and Blood Vessels and Spleen

TREATMENT OF PATENT DUCTUS ARTERIOSUS. J. EXALTO and J. C. TUMMERS, Nederl. tijdschr. v. geneesk. **86**:2772 (Nov. 7) 1942.

Reports are given concerning 3 patients with patent ductus arteriosus; 2 of them were operated on. During operation the heart of the first child stopped beating, causing death. The second patient, a girl of 19 months, recovered after the operation (she is the youngest patient in literature who was cured in this way). In the third patient, a boy of 11, no immediate indication for operation was present.

VAN CREVELD, Amsterdam, Netherlands.

DETERMINATION OF ELECTROCARDIOGRAPHIC POINTS OF IMPORTANCE. A. C. M. LIPS, Nederl. tijdschr. v. geneesk. **86**:2837 (Nov. 14) 1942.

A graph is described by means of which the various points of importance of the electrocardiogram can quickly be read in a simple way.

VAN CREVELD, Amsterdam, Netherlands.

PATHOLOGIC CHANGES IN GAUCHER'S DISEASE. R. VAN DAM, Nederl. tijdschr. v. geneesk. **86**:2974 (Nov. 28) 1942.

The pathologic and anatomic findings in a patient who died of Gaucher's disease are described. There were extensive changes in the liver, the spleen and the bone marrow. The author stresses the fact that the endothelial cells of the spleen do not collect kerasin. This case offers no support to Epstein's hypothesis which implies that Gaucher's disease is caused by hypofunction of the suprarenal gland.

VAN CREVELD, Amsterdam, Netherlands.

SOME MALFORMATIONS OF THE CORONARY ARTERIES OF THE HEART. F. H. TER POORTEN, Nederl. tijdschr. v. geneesk. **86**:3193 (Dec. 19) 1942.

An infant 2½ months old showed symptoms of gastroenteritis and bronchopneumonia. After some days the child had attacks of cyanosis and dyspnea and died. At necropsy severe changes in the heart muscle were found, caused by an abnormal origin of the left coronary artery, which originated from the pulmonary artery. The author gives a short description of the clinical course in cases in which there was this abnormality. At present 15 such cases are known, but none of them were recognized during the life of the patient. In 12 of these cases of malformation of the left coronary artery death occurred within the first year of life. Degeneration and necrosis of the heart muscle as the direct causes of death occur in such cases when no compensatory collateral circulation develops. Three other patients who had no complaints of malformation died when they were 38, 53 and 64 years old, respectively, but none of them died from heart disease. At necropsy the heart muscle was normal in all 3 cases, whereas there existed distinct symptoms of compensated circulation of the heart muscle (enormous dilatation of the coronary arteries). Such a compensation also was found in 2 cases of malformation of the right coronary artery.

The author enters into a detailed discussion of the formal genesis of the malformation of the coronary arteries, especially of the left one. He gives his own explanation of the fact that an abnormal left coronary artery occurs more frequently than an abnormal right one. This malformation probably develops in an early stage of the fetal development.

Finally a short discussion is given of the cases in which the right coronary artery was more dilated than the left one, and of the clinical significance of this dilatation.

VAN CREVELD, Amsterdam, Netherlands.

CAROTENE–VITAMIN A METABOLISM, THE PROTEIN SPECTRUM AND THE RETICULO-ENDOTHELIAL SYSTEM OF ASCHOFF. L. A. G. HISSINK, Nederl. tijdschr. v. geneesk. **86**:3200 (Dec. 19) 1942.

In his consideration of a patient with postoperative carotene icterus, vitamin A deficiency, endocrine disorders and an altered protein spectrum, the author tries to show the significance of the reticuloendothelial system for the metabolism of carotene–vitamin A and for that of the proteins, and attempts to demonstrate that this system eventually is influenced by endocrine disturbances. It is a remarkable fact that after large doses of vitamin A were administered the protein level returned to normal values.

VAN CREVELD, Amsterdam, Netherlands.

LYOPHILE DRYING OF BLOOD PLASMA AND OF BREAST MILK. G. G. MASTENBROEK and C. VAN DER REYDEN, Nederl. tijdschr. v. geneesk. **88**:565 (June 17-24) 1944.

The authors describe a modification of the technic for the preparation of lyophile plasma given by Flosdorf and Mudd. Like Greaves and Adair (1939) they replace the condenser in the refrigerating mixture with a condenser in which the evaporating spiral of a refrigerator is built. The blood is centrifuged in such a way that 62 to 67 per cent citrated plasma (90 cc. of a 3.3 per cent solution of sodium citrate in 500 cc. of blood) is obtained. To prevent the fats, agglutinated by the process of drying, from remaining agglutinated when the dried plasma is redissolved, the plasma before being dried is diluted with a sterile 40 per cent solution of dextrose in the proportion of 1 to 7. Full details of the technic are given. Indications for plasma transfusion are discussed. With the technic used for the lyophile drying of blood plasma breast milk also was dried. The provisional results of the analysis and of the practical use of this dried breast milk are given.

VAN CREVELD, Amsterdam, Netherlands.

VISCOSITY OF BLOOD DURING CLOTTING. H. C. BURGER and P. H. VAN CITTERT, Nederl. tijdschr. v. geneesk. **88**:760 (Aug. 12-19) 1944.

The authors describe a mechanical method by which during the process of clotting the viscosity can be measured, while the clotting process itself is practically unaffected by the mechanical treatment. Only a small quantity of blood (about 150 mm.) is required for this method.

A small amount of fresh blood is placed in a small basin which is ground in the form of a globular segment in a plate of glass or some other material. The basin which contains the blood is mounted on a ground plate, which turns round an axle. A lantern projects a small ray of light on the surface of the blood. The reflected ray of light is projected on a scale or on a photographic registering apparatus. The whole apparatus is turned every half minute for three seconds at an angle of about 5 degrees. This displacement of the ray of light gives a curve in which the length of the waves is a measure of the viscosity. When the blood has clotted the length of the wave is zero. It appears in this investigation that the clotting takes place more slowly when the amount of blood is larger. Therefore in comparative studies always the same quantity of blood should be taken.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of Nose, Throat and Ear

THE TREATMENT OF ACUTE SUPPURATIVE OTITIS MEDIA WITH PENICILLIN. LOUIS WEINSTEIN and HILTON B. ATHERTON, J. A. M. A. **129**:503 (Oct. 13) 1945.

In 50 cases of acute suppurative otitis media (48 occurring as complications of scarlet fever) the patients were treated with intramuscular injections of penicillin, 10,000 units every three hours until the external auditory canal had been

dry for at least twenty-four hours. In 82 per cent of the cases the ear was dry in less than four and one-half days. Recurrence was noted in 16 per cent of the cases. These responded to larger doses of the drug. Two patients had peripheral facial paralyses which gradually cleared. One patient had phlebitis of a lateral sinus. Two patients had elevated temperatures attributed to penicillin allergy. No mastoid infections required surgical treatment.

Infections with Staphylococcus aureus alone or in combination with streptococci seemed to require larger doses. Infections with gram-negative bacteria responded to local treatment with a solution of 10 per cent ethyl carbamate and 1 per cent sulfanilamide.

The treatment recommended for acute otitis media is the intramuscular administration of penicillin in doses of 15,000 units every three hours from the time of the first appearance of exudate until the ear has been dry for seventy-two hours.

BAIRD, Wauwatosa, Wis.

LOCAL USE OF PENICILLIN IN INFECTIONS OF THE EAR, NOSE AND THROAT: RESULTS OF TREATMENT. FLETCHER D. WOODWARD and THOMAS HOLT, J. A. M. A. **129**:589 (Oct. 27) 1945.

Local treatment with penicillin was accomplished by use of (1) a solution of 500 units of sodium penicillin per cubic centimeter of isotonic solution of sodium chloride, (2) a water-soluble jelly containing 1,000 units per gram and (3) lozenges containing 800 units per lozenge. Application was by instillation of drops into the ear, by spraying and instillation of jelly into the nose, by lavage (if indicated) of the sinuses followed by the instillation of jelly, by slow dissolution of the lozenges on the tongue for infections of the mouth and gums and by lozenges combined with spraying of the throat for throat infections.

The local use of penicillin proved helpful in combating acute and subacute infections except acute otitis media. It was found helpful in some cases of chronic otitis media but of no value in chronic sinusitis. Combined treatment with systemically administered penicillin or with appropriate sulfonamide compounds enhanced the therapeutic effect. Local treatment did not produce any dramatic change in the bacterial flora of the nose and throat.

BAIRD, Wauwatosa, Wis.

CONTROL OF AIR-BORNE INFECTION, PARTICULARLY THE COMMON COLD. SVERRE QUISLING, Wisconsin M. J. **44**:1070 (Nov.) 1945.

A colloidal preparation of acetylsalicylic acid, specially ground so that the particles averaged 0.1 micron in size, was found to have increased germicidal power as compared to ordinary preparations, in which the particles are 14 microns or more in size. The colloidal preparation was also found less irritating to mucous membranes, and it did not produce any perceptible change in blood clotting time or prothrombin. High chemical stability, low toxicity and convenience of administration are additional advantages of the drug.

The correlation between the caliber of the openings of the ducts in the skin and mucous membranes, the size of the virulent organisms and the size of the particles of the drug is pointed out. Penetration into the infected ducts may partially explain the action of the colloidal solution.

Treatment in the early stages of a "cold" was given to 200 patients. This consisted of inhaling two to three breathfuls of the colloidal powder two or three times daily for several days. Duration of the colds was decreased, and complications were much less frequent.

BAIRD, Wauwatosa, Wis.

DIFFICULTIES IN REMOVING SOME FOREIGN BODIES FROM THE LOWER AIRWAYS. C. DYKSTRA and C. VERSTEEGH, Nederl. tijdschr. v. geneesk. **88**:149 (Feb. 12-19) 1944.

In order to localize a foreign body in the airways at least two roentgenograms are necessary, an anteroposterior roentgenogram and one exactly perpendicular to the anteroposterior roentgenogram. Such an exact localization is especially important for the bronchoscopist if the foreign bodies are small. This is illustrated by 2 cases observed by the authors. In both cases the foreign body had penetrated into the ventral branches of the bronchial tree, probably because the ventral parts of the lung are best ventilated and the sucking power is greatest in the ventral direction. Both cases had a benign course. In a third case pneumonotomy had to be performed in order to remove the foreign body (a screw), which had caused atelectasis. After the pneumonotomy the lung expanded quickly and completely, and no pleuritis arose notwithstanding the fact that at the operation a small quantity of pus was removed from the bronchus. In a fourth case the foreign body (also a screw) had caused a marked stricture of the lumen of a large bronchus with bronchiectatic changes in the right lower lobe. After a "cutting" lobectomy had been done the patient recovered.

VAN CREVELD, Amsterdam, Netherlands.

A CASE OF OTITIS MEDIA WITH THE GRADENIGO SYNDROME. F. H. QUIX, Nederl. tijdschr. v. geneesk. **88**:796 (Aug. 26-Sept. 2) 1944.

This is the report of a case in which the patient was a boy of 14 years, with critical remarks on the indications for and the technic of operation for petrositis. The significance of chemotherapy in such cases is stressed.

VAN CREVELD, Amsterdam, Netherlands.

LOCAL CHEMOTHERAPY IN OTOLOGY, RHINOLOGY AND LARYNGOLOGY. P. R. BAARSMA, Nederl. tijdschr. v. geneesk. **88**:157 (Feb. 12-19) 1944.

The results obtained by local application of sulfanilamides in diseases of the nose, the ear and the sinuses and in infections of the lower airways, especially bronchiectasis and chronic bronchitis, are described. On the whole the results were favorable, especially in the cases of acute disease. For this local treatment those cases of bronchiectasis were reserved in which surgical treatment had to be excluded. First the secretion had to be sucked off. Then the patient coughed repeatedly. After that 50 to 100 cc. of a 5 per cent solution of sulfathiazole was introduced into the airways at the affected side by means of a half soft catheter. In cases of chronic bronchiectasis such a treatment was performed twice a week, or during one week the sulfathiazole solution was introduced twice a day by means of the aspiration method of Singer.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of Lungs, Pleura and Mediastinum

ANNULAR AREAS OF PULMONARY RAREFACTION IN CHILDREN. EILEEN PHILLIPS and CHESTER A. STEWARD, New Orleans M. & S. J. **98**:247 (Dec.) 1945.

In the past pulmonary cysts were considered rare. With increasing use of roentgen rays annular shadows are now not infrequently found. Studies of these cases show that cysts or cystlike changes may be of three types. They may be of congenital origin, single or multiple and large or small. In these cases there is no previous history of respiratory infection or aspiration of foreign bodies, and the condition does not spontaneously clear up. The cysts or cystlike changes may be of bronchiectatic type. There may or may not be a history of inhalation of a foreign body, although a foreign body is the usual cause. In the event of infection in either of these conditions, removal of the involved area is necessary for recovery. The cysts may be pneumatoceles and cavities remaining after the evacuation of

pulmonary abscesses. These are inclined to disappear spontaneously. Prolonged observation often is the only method of segregating this type from classes 1 and 2. Case histories are presented illustrating each type described.

BERKLEY, Beverly Hills, Calif.

ON THE OCCURRENCE OF NECROSIS AND ON THE CAUSE OF DEATH IN CASES OF PNEUMONIA TREATED WITH SULFAPYRIDINE. I. J. ZELDENRUST and J. D. VERLINDE, Nederl. tijdschr. v. geneesk. **86**:2520 (Oct. 10) 1942.

An account is given of the occurrence of necrosis of inflamed lung tissue in 4 cases of fatal pneumonia, in which the patients were treated with sulfapyridine. The possibility is considered whether this necrosis is the result of local anaphylaxis and whether the fatal results were entirely or partly the consequences of general anaphylaxis.

VAN CREVELD, Amsterdam, Netherlands.

ON THE OCCURRENCE OF NECROSIS AND ON THE CAUSE OF DEATH IN CASES OF PNEUMONIA TREATED WITH SULFAPYRIDINE. II. J. D. VERLINDE and J. ZELDENRUST, Nederl. tijdschr. v. geneesk. **86**:2574 (Oct. 17) 1942.

Basing their theory on experiments with rabbits the authors maintain that the cause of death of human beings with pneumonia which has been treated with sulfapyridine can be a general one, and that the necrosis in the lungs is a local, anaphylactic reaction. Rabbits can be sensitized with filtrates prepared from the infected lungs of rabbits. The reinjection of a large quantity of such an extract (5 cc.) can cause death by shock. Extracts from lungs of rabbits which have been treated with sulfapyridine can cause death by shock with even a tenth of this quantity. Rabbits which have recovered from pneumonia are probably also sensitized. In these animals shock occurs after one injection of a large quantity of lung extract from an uninfected rabbit just as well as after the injection of a large quantity of lung extract from a rabbit which has been treated with sulfapyridine. A chemicospecific anaphylaxis against sulfapyridine could not be demonstrated.

VAN CREVELD, Amsterdam, Netherlands.

UNUSUAL PNEUMONIA IN INFANTS. A. F. A. S. VAN WESTRIENEN, Nederl. tijdschr. v. geneesk. **87**:197 (Jan. 30) 1943.

The cases of 2 infants suffering from unusual forms of pneumonia are discussed. The first baby had a pulmonary complication caused by virus influenza. In this case there was a nearly complete atelectasis of the right lung, which persisted for many months and which could be recognized clinically and roentgenologically. Besides this there was a partial emphysema. The changes closely resembled those found in mice which are infected with human influenza virus (Straub, 1940).

The second infant had a toxic pneumonia with multiple abscesses in the lungs with symptoms of bilateral involvement of the pleura, which was already present on the first day of the disease. This early occurrence of pleural inflammation is characteristic of this unusual form of pneumonia in infancy (Nassau, 1926). One must wait for the results of modern chemotherapy in these cases of pneumonia with purulent pulmonary abscesses which have such a fulminating course.

VAN ÇREVELD, Amsterdam, Netherlands.

Diseases of the Gastrointestinal Tract, Liver and Peritoneum

GALACTOSEMIA WITH HEPATIC DAMAGE. SHERMAN MELLINKOFF, BERNARD ROTH and JAMES MACLAGGAN, J. Pediat. **27**:338 (Oct.) 1945.

There have been 4 previously reported cases of galactosemia with hepatic damage. In this disease the infant's liver is apparently unable to convert galactose

into glucose. Galactosemia and galactosuria are thus produced, and this condition may be associated with severe hepatic disease. The latter is rapidly cured when galactose is removed from the diet.

An instance of this disorder was discovered in a 2 month old white American baby whose appearance was strongly suggestive of hepatic cirrhosis. The abdomen was swollen with half a liter of ascitic fluid, and the liver reached the umbilical level. The skin over the abdomen was tight and shiny, and the superficial veins were greatly engorged. There was pitting edema from feet to knees.

The baby was anemic and had a high blood sugar level and a low plasma protein level, and a cephaline flocculation test gave a result of 4 plus. The urine was remarkable only for a moderate amount of protein and large quantities of galactose. The latter was suspected because the urinary sugar was not fermented by yeast in sixteen hours. Galactose was identified by other biochemical tests.

Lactose, practically the sole source of galactose in the diet, was eliminated by feeding the baby Nutramigen, a synthetic food containing casein hydrolysate and maltose. Rapid recovery ensued. In ten days ascites and edema were gone, and in six months the child was normal and healthy in all respects except for a palpable liver. Anemia, hypoproteinemia, proteinuria, galactosemia and galactosuria all disappeared, and the cephalin flocculation test gave a negative result.

The following hypothesis is suggested to explain the facts: Galactose cannot be utilized because of an inborn error of metabolism. This sugar therefore accumulates in the blood and is deposited in the liver, either as galactose itself or as some polymer of galactose. This causes reversible hepatic damage. The proteinuria may be a result of renal damage from the galactose, or it may simply indicate the production of some abnormal plasma protein. AUTHORS' ABSTRACT.

HYPERTROPHIC PYLORIC STENOSIS (ANALYSIS OF THIRTY-SEVEN CASES AT CHARITY HOSPITAL). L. J. O'NEIL, New Orleans M. & S. J. **98**:287 (Dec.) 1945.

The author reviews 37 cases of pyloric stenosis in which operation was performed. Attention is directed to 19 consecutive cases in which there were no deaths, for which result efficient preoperative preparation and prompt surgical relief are given the credit. BERKLEY, Beverly Hills, Calif.

ETIOLOGY AND PATHOGENICS OF APPENDICITIS. E. HUSTINX, Nederl. tijdschr. v. geneesk. **86**:2840 (Nov. 14) 1942.

In the writer's opinion the primary cause of appendicitis is the occlusion, and the secondary is the infectious process. The process of occlusion is favored by the small dimension of the appendix and by the thickening of the feces. He tries to prove that a diet rich in meat has an influence on the length of the intestine and on that of the appendix in particular. Meat diet, in addition to a lack of activity on the part of modern people, is a cause of chronic constipation. The narrowness of the appendix and the thickening of the feces are the cause of a storage of feces in the appendix. This mass of feces causes appendicular colic. When the mass of feces results in occlusion, the process of infection starts, and then appendicitis must follow. VAN CREVELD, Amsterdam, Netherlands.

SPONTANEOUS HYPOGLYCEMIA IN A CHILD. W. DRUKKER, K. B. TJIOOK and H. L. VAN BEUSEKOM, Nederl. tijdschr. v. geneesk. **87**:67 (Jan. 9) 1943.

A girl 7 years old had spontaneous hypoglycemia, caused by an adenoma of the pancreas. After removal of the adenoma the child became normal. The authors give a short review and a more detailed discussion of the differential diagnosis between functional and organic hyperinsulinism. There is a brief discussion of the therapy of both forms. VAN CREVELD, Amsterdam, Netherlands.

ACETONEMIC CONVULSION IN CHILDREN AND HYPOGLYCEMIA. J. R. BORST and L. J. VAN NIEROP, Nederl. tijdschr. v. geneesk. **88**:19 (Jan. 1-8) 1944.

Some cases of acetonemic vomiting in childhood are combined with convulsions. If there is necropsy in such cases the changes in the liver are found to resemble those occurring in an acute severe intoxication such as is caused by chloroform. The clinical picture of these cases of acetonemic vomiting combined with convulsions varies, and severe diagnostic difficulties may arise. Opinions differ on the mechanism of the convulsions in such cases and on the relation between the convulsions and the accompanying hypoglycemia if such a relation does exist. The authors describe a typical case of acetonemic vomiting combined with convulsions in a girl 4½ years old; the quick recovery after administration of sugar in this case was remarkable. It was assumed that in this case the convulsions had appeared spontaneously.

VAN CREVELD, Amsterdam, Netherlands.

THE CONSERVATIVE TREATMENT OF PROLAPSUS ANI ET RECTI IN YOUNG CHILDREN, H. F. WIERS, Nederl. tijdschr. v. geneesk. **88**:518 (June 3-10) 1944.

In 1942 and 1943 the author observed a total of 21 cases of prolapsus ani et recti, in all of which the patients were treated in the conservative way with success. No use had to be made of the operative treatment or of a treatment with injections as recently had been recommended from the surgical side. The author is of the opinion that the increase of the number of cases of prolapsus ani et recti in recent years is related to the increasing pedagogic difficulties and the modified feeding and feeding conditions. Especially the use of large amounts of potatoes often gives rise to chronic intestinal catarrh, which in its turn may promote the appearance of a prolapse. The treatment of a number of patients is discussed.

VAN CREVELD, Amsterdam, Netherlands.

CONTRAINDICATIONS TO LIVER PUNCTURES. A. J. C. HAEX, Nederl. tijdschr. v. geneesk. **88**:672 (July 15-22) 1944.

The following contraindications to liver puncture as introduced by Iversen and Roholm (1939) are mentioned: (1) a disturbance in one of the factors necessary for the normal clotting of blood; (2) existence of fever with jaundice, and the presence of colon bacilli in the duodenal fluid; (3) existence of an intercurrent infection; (4) asthenia (usually); and (5) pleuritis dextra.

If a diagnostic puncture is desirable in a child with an enlarged liver (e. g., glycogen disease), then aspiration biopsy via the abdominal wall is recommended.

The puncture always should be performed with all precautions for asepsis and always should be done in the posterior axillary line and not too low. One has further to keep in mind the possibility of a situs inversus.

VAN CREVELD, Amsterdam, Netherlands.

Nervous Diseases

SPINAL CORD TUMORS IN CHILDREN: A STUDY OF THREE CASES OF EPENDYMOMA. AARON NISENSON and GEORGE H. PATTERSON, J. Pediat. **27**:315 (Oct.) 1945.

Children with early signs of pressure on the spinal cord present difficult diagnostic problems and are usually given an incorrect diagnosis. Three cases of ependymoma of the spinal cord in children are presented. A review of these cases brings to light signs and symptoms which should be of benefit in more accurate diagnosis.

The first case is that of a 12 year old boy with pain and stiffness of the back for one and a half years. The pain was worse at night. For eight months he was treated conservatively without relief. A spinal puncture revealed xantho-

chromic fluid and a block on jugular compression. After surgical treatment followed by roentgen ray therapy the boy has been asymptomatic for three and one half years, despite incomplete surgical removal of the tumor.

In the second case, a 4½ year old boy was treated at first for poliomyelitis. Subsequently there was rapid progression of an ependymal tumor which in one year involved the brain and the entire spinal cord. The outstanding feature was a painful rigid spine which did not relax under anesthesia and repeated dry spinal punctures.

The third case is that of a 13 year old boy who complained of pain in the back for three months. The pain was worse at night and was aggravated by sneezing and coughing. The patient was first given a diagnosis of tuberculosis of the spine and later of poliomyelitis. Spinal puncture revealed an elevated total protein, and injection of iodized poppyseed oil 40 per cent confirmed the diagnosis of tumor of the spinal cord.

In these cases pain and stiffness of the back, slowly progressive and usually worse at night, were prominent symptoms. Coughing and sneezing may increase the pain. Some degree of weakness of the lower extremities was evidenced at some time during the course of the illness.

Spinal puncture was found to be the most important diagnostic procedure and is recommended early when the diagnosis is doubtful and a roentgenologic examination is noncontributory. Compression of the pedicles when observed on roentgenologic examination was found to be a valuable contributory finding.

Surgical removal should be attempted, even in the face of extensive involvement. One of these patients is still alive and asymptomatic after three and a half years.

AUTHORS' ABSTRACT.

DILATATIO CAVI VENTRICULI SEPTI PELLUCIDI. C. DE LANGE, Nederl. tijdschr. v. geneesk. **86**:2507 (Oct. 10) 1942.

This is the case history of a premature (8 month old) child with a weight at birth of 3,100 Gm. and with a large-sized head. The child proved to be mentally backward, but no definite neurologic symptoms could be stated. The infant died at the age of 10 months.

It was found at necropsy that the right lung had only two lobes and, that there was a hypertrophia cerebri, a rather large-sized adenohypophysis and a wide open empty cavum septi pellucidi.

Microscopic examination revealed that the inner wall of the cavum was lined with cells resembling cells of the ependyma and called pericaval cells by Wolf and Bamford. With these authors de Lange is of the opinion that these cells are modified glial cells. Otherwise the brain proved to be normal. The anomaly may be explained as a process of retardation combined with a slight malformation. The roentgen diagnosis of the open cavum septi pellucidi is discussed.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of the Genitourinary Tract

THE TOTAL AMOUNT OF LEAD IN THE URINE. C. P. VAN DYK, Nederl. tijdschr. v. geneesk. **86**:3141 (Dec. 12) 1942.

The former method of determining the amount of lead in the urine by coprecipitation with calcium oxalate, which shows only the inorganically bound lead, can be replaced by a simple method which estimates the entire amount of lead in the urine. The amount of 100 micrograms of lead per liter of urine is still regarded as a normal value.

VAN CREVELD, Amsterdam, Netherlands.

THE HORSESHOE KIDNEY. M. W. VAN WEEL, Nederl. tijdschr. v. geneesk. **87**:61 (Jan. 9) 1943.

The horseshoe kidney is discussed. A report is made of a case in which a pelvic stone was removed and of another case in which the appearance of a pyonephrosis required a heminephrectomy.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of the Ductless Glands; Endocrinology

ADRENOGENITAL PSEUDOHERMAPHRODITISM TREATED WITH STILBESTROL. C. BERKELEY MCINTOSH and WILLIS E. BROWN, J. Pediat. **27**:323 (Oct.) 1945.

A 5 year old patient was referred to the University hospital for diagnosis of a condition characterized by a rapid rate of growth and hermaphroditism. The child's measurements were those of an average 7½ year old girl. The physical findings included a masculine type of physique, hirsutism of the legs and abnormal genitalia. The phallus measured 2.5 inches (6.4 cm.) and had a definite glans and a prepuce but no urethral opening. The latter was in a completely hypospadiac position. There were well developed labia present. The vaginal orifice was small and partially obliterated. The androsterone content of the urine was increased to 22 mg. equivalents (normal from 4 to 8) in a twenty-four hour sample. Exploratory laparotomy showed the presence of normal tubes and ovaries, a rudimentary uterus and generalized enlargement of both adrenal glands. Microscopic examination of the gland revealed diffuse hyperplasia of the cortex. A diagnosis of adrenogenital female pseudohermaphroditism was thus established.

Attempts were made to feminize the patient. Roentgen therapy was tried first and without success. Diethylstilbestrol was then employed in dosages ranging from 5 mg. to 1 mg. a day. This was continued for two years. The results of this therapy, although definite, were disappointing. The female secondary sex characteristics were accentuated, as shown by the development of breast tissue and the disappearance of hirsutism. The effect on the clitoris was only a minimal reduction in size. The effect on the growth of the child was difficult to evaluate. The growth rate was normal for the interval during which the patient received diethylstilbestrol, although it had been rapid before that time, and bone age determinations before and after endocrine therapy showed no acceleration of the bone ages. Other authors have reported, however, that untreated pseudohermaphrodites grow rapidly during the first few years and that then the growth is terminated early so that their final height is considerably less than average. The authors are inclined to believe that the deacceleration of growth rate in this patient was only coincidental with the endocrine therapy. After administration of estrogen had been discontinued, plastic operations were performed. These consisted of an amputation of the clitoris and an extension of the vaginal orifice. It was thought that when the girl becomes 15 or 16 years old, and it is more desirable for her to have well developed sex characteristics, estrogen therapy may again be indicated.

It is noteworthy that this patient had a female sibling who was likewise a pseudohermaphrodite. Since animal experimentation indicates that such congenital anomalies may be due to antepartum endocrine dysfunction in the mother, the androgen excretion of the mother of the patient was determined. It was found to be normal in amount.

AUTHORS' ABSTRACT.

ENDOCRINE DISTURBANCES OF PUBERTY. A. MARTEL, Union méd. du Canada **72**: 369 (April) 1943.

Normal puberty follows a definite pattern and is subject to the production of endocrines. There are two phases, one of growth in stature and weight and the other of development of sex characteristics.

In chronologic order the glands which influence puberty are the thymus, the pituitary (growth fraction), the thyroid, the parathyroid and the adrenal. Then the anterior lobe of the pituitary gland produces gonadotropic hormones, bringing into action the ovaries or testes.

Deviation of statural growth may be hypotrophic (primordial infantilism, Paltauf's dwarfism, Levi-Lorrain syndrome, Souqes-Chauvet infantilism, or Brissaud's dwarfism, or hypertrophic simple gigantism or Hutinel's type). Obesity may be the simple type of Fröhlichs syndrome.

Genital overgrowth may be caused by precocious puberty, ovarian tumor, adrenal tumor or testicular tumor. Retarded maturity may be due to hypothyroidism or to ovarian deficiency. In boys, cryptorchidism may be mechanical or hormonal.

The thyroid gland is involved in many of these syndromes, and may also produce specific examples of overactivity (toxic goiter) or underactivity (adolescent hypothyroidism).

DAFFINEE, Melrose, Mass.

Diseases of the Muscles, Bones, Joints and Lymph Glands

MYOSITIS OSSIFICANS PROGRESSIVA. KERMIT J. RYAN, J. Pediat. **27**:348 (Oct.) 1945.

Myositis ossificans progressiva is a peculiar disease of the locomotor system occurring in the growth period of children. It affects not only the muscles, but tendons, ligaments, fasciae and aponeuroses, and is characterized by the appearance in them of masses of bone or of areas of calcification. It has periods of exacerbation and regression, and is commonly associated with various congenital anomalies, the commonest being malformation of the great toes.

There is no definite etiology; various theories have embraced heredity, rheumatic infection and trauma in susceptible people. The disease usually starts after infection or trauma, and parents notice small, soft, cystlike masses over different parts of the body; later, whole muscle areas calcify and form bone. In general, all laboratory work is negative in result except roentgenologic examination, which reveals the true identity of the process. There is no treatment, and the prognosis is grave. These children usually succumb before 15 years of age as a result of involvement of the muscles of respiration. Pneumonia or tuberculosis may intervene.

This case report resembles most of the others except that it is one among the 25 per cent in which the disease was not associated with a congenital anomaly. The child was first seen in November 1941 with fever associated with swollen and painful joints. A diagnosis of rheumatic fever was made at that time, and the patient was treated with bed rest and acetylsalicylic acid. Over a period of months the child's joints became stiffer, and he lost 11 pounds (5 Kg.). Examination in May 1942 revealed an undernourished youngster who appeared chronically ill. On walking the child bent forward in a fixed position with a stiff spine and was quite unsteady. There were atrophic changes in all muscles, and the fingers were fusiform. All other joints revealed limitation of motion and were quite painful with moderate swelling. A diagnosis of atrophic arthritis was made, and general symptomatic treatment followed. Tonsillectomy and adenectomy were advised, but because of persistent gingivitis, it was decided to send the child for dental care, to return to the hospital and have a tonsillectomy and adenectomy later.

In December 1943 he was again seen, and at that time there was a cystlike tumor in the left axilla and a large area of induration on the posterior aspect of the thigh. A roentgenologic examination revealed bone formation in the muscle.

In this case the myositis ossicans has followed the usual course, the malady beginning as an attack of acute rheumatism with progression, and continuing with a partial ankylosis of the neck, the shoulders and the spine and with the formation of bony layers. The nature of the dystrophy is still obscure, and the treatment is unsatisfactory.

AUTHOR'S ABSTRACT.

EPICONDYLITIS HUMERI AND ITS TREATMENT BY MEANS OF LOCAL INJECTIONS OF HISTAMINE. R. K. W. KUIPERS, Nederl. tijdschr. v. geneesk. **87**:105 (Jan. 16) 1943.

The description of the symptoms of epicondylitis humeri is followed by some remarks concerning the causation and pathogenesis of this clinical picture. The author gives arguments in favor of the conception that epicondylitis and the exertion pains in general should be regarded as rheumatic conditions. He mentions favorable results obtained in this disease by local injections of histamine.

VAN CREVELD, Amsterdam, Netherlands.

Surgery and Orthopedics

TWO METHODS FOR PLACING A CENTRAL NAIL, ESPECIALLY IN THE DIAPHYSEAL SIMPLE FRACTURES. EDUARDO GÓMEZ JÁUREGUI, Bol. méd. d. hosp. inf. **2**:289 (Nov.-Dec.) 1945.

The author describes and discusses the different methods and materials used by different orthopedists in the reduction of simple fractures. Some of those methods are difficult and are not always successful in accomplishing the reduction of the fractures.

The author has conceived two modifications to the classic methods.

In the angular traction method, he produces a hole in the shaft of one segment and introduces a stout string that is tied to the nail which is pulled in place after the fracture is reduced.

The "bolting" method is modified by introducing the whole nail in the bone marrow of one segment. The two segments are held one in front of the other, but separated 1 or 2 cm. by means of traction. Then, a slender forceps being introduced through the separation, half of the nail is pushed through the bone marrow of the other segment. The traction is then stopped, and the fracture held by means of a cast.

MADERO, México, D. F., Mexico.

THE IMPORTANCE OF EARLY TREATMENT OF THE FLATFOOT. G. CHAPCHAL, Nederl. tijdschr. v. geneesk. **87**:208 (Jan. 30) 1943.

A short discussion of the congenital flatfoot is followed by a discussion of the mechanism of the flatfoot which is acquired at an early age. The author stresses the importance of early treatment of the static flatfoot. A review of the therapeutic possibilities is given.

VAN CREVELD, Amsterdam, Netherlands.

TREATMENT OF BURNS WITH TANNIC ACID POWDER. J. BOL, Nederl. tijdschr. v. geneesk. **88**:534 (June 3-10) 1944.

Instead of treating burns with tannic acid compresses or of spraying the burns with a solution of tannic acid, the author made use of tannic acid powder. After the blister has been opened and the more or less loose epidermis has been removed the surface of the wound is carefully rubbed dry. Then a thin layer of tannic acid powder is spread on the wound by means of a piece of cotton or powdered on the wound by means of a small apparatus. After fifteen to twenty minutes a thin layer appears on the surface of the burn; when there is a pronounced secretion on the wound sometimes it is necessary to use a fan in order to obtain quick drying of the layer. Then this tannic acid layer is richly powdered with talcum. No bandage is applied, except for young children who get a dry richly talcum-powdered bandage. The favorable result of this treatment is striking; no etching effect of the tannic acid powder is observed, as the dissolved tannic acid probably immediately is bound by the protein of the superficial cell layers, which in this way are shut off from the air. Except in 1 case no other treatment of the burns than the powdering with tannic acid powder was necessary.

VAN CREVELD, Amsterdam, Netherlands.

Miscellaneous

SOME PRINCIPLES OF GENETICS. HAROLD CUMMINS, New Orleans M. & S. J. **98**:252 (Dec.) 1945.

The author discusses the value of the studies of genetics to the physician. Polycythemia, hemolytic icterus, hemophilia and a variety of anomalies are cited as examples of medical problems worthy of genetic study. Factors of heredity may determine conditions of health, some malformations and predispositions to disease. Some characteristics which seem inflexibly to be determined by heredity are blood groups, eye color and Huntington's chorea. Other characteristics are hereditarily labile. The discussions on heredity, environment and constitution and their relationship to health and disease and to malformations and traits is both interesting and informative.

BERKLEY, Beverly Hills, Calif.

INTOXICATION BY MUSHROOMS: CAUSE, SYMPTOMS AND TREATMENT. L. W. VAN ESVELD, Nederl. tijdschr. v. geneesk. **86**:2766 (Nov. 7) 1942.

Since at present so many people are seeking mushrooms who do not have sufficient knowledge of the poisonous ones, the chance of poisoning has greatly increased. This article discusses the active parts of mushrooms and the symptoms and treatment of poisoning. Only in cases of intoxication from Inocybes (poisoning by pure muscarine) is causal therapy possible. For the symptomatic treatment of poisoning caused by certain varieties (Amanita phalloides) special measures are necessary.

VAN CREVELD, Amsterdam, Netherlands.

A NEW PREPARATION FOR THE TREATMENT OF PATIENTS WITH SHOCK, "CAPAINE." L. A. G. HISSINK, Nederl. tijdschr. v. geneesk. **88**:521 (June 3-10) 1944.

Brinkman by means of papayotin derived from casein has made a liquid with a high content of polypeptides. It appeared that a 10 per cent solution of this casein hydrolysate, named by Brinkman "Capaine," has a colloid-osmotic pressure 4 to 5 times as great as that of blood. The author studied the value of this solution in the treatment of a number of patients with shock and obtained good results. Usually he gave 75 cc. of a 15 per cent solution of "Capaine" diluted with a 0.9 per cent solution of sodium chloride or a 5 per cent solution of dextrose in 1,000 cc. of fluid. In cases of severe shock he gave the patient 150 cc. of the "Capaine" solution in 1,000 cc. of fluid. The tempo of the injection depends on the blood pressure; a low blood pressure requires a more rapid infusion. When the heart is normal there is no objection to injecting several liters of fluid in a patient with shock. Besides the good effect of the injection now and then there were other temporary nondangerous effects, especially when more than 100 cc. of a 15 per cent solution of "Capaine" was injected within one hour.

VAN CREVELD, Amsterdam, Netherlands.

Society Transactions

CHICAGO PEDIATRIC SOCIETY

Louis W. Sauer, M.D., *President, in the Chair*

Oct. 16, 1945

SEMINAR DISCUSSION ON IRRADIATION THERAPY OF TONSILS AND ADENOIDS

Pediatric Aspects. DR. PHILIP ROSENBLUM.

It is probably no overstatement to say that tonsillectomy is the most frequent operation performed in this country, or that tonsils are removed more frequently for diseases they are apt to produce than for harm they are actually doing. There is no doubt that a large group of patients suffering from recurrent infections of the upper respiratory tract are benefited by tonsillectomy. However, it has been shown by thorough follow-up examinations among a large group over a period of years that frequently the anticipated benefits were not attained. The need of the individual patient, based on impressions gathered from considerable experience, should be the criterion on which decision is based.

My associates and I do not feel that all tonsils are or should be amenable to roentgen therapy; nor do we feel that all tonsils should be removed surgically. In our experience there are two forms of hypertrophy of the tonsils: that in which all the anatomic structures of the tonsils become more or less hypertrophied and that in which the crypts and lacunas become distended by secretion. The soft variety is more frequent in children. Soft tonsils with wide open crypts have offered the best results in this series, whereas large pedunculated tonsils do not respond as well.

Roentgenologic treatment of tonsils and adenoids has passed the experimental stage but has definite indications as well as contraindications; it is not a panacea for all tonsillar and adenoidal infections. The pediatrician often is confronted with the problem of an infant or young child who has such infections repeatedly. Irradiation offers a definite form of treatment, which may be done sometimes months before the child is ready for surgical intervention, and not infrequently may prevent more serious complications. It has the following advantages: The tonsils are preserved, and the entire infectious area is attacked. No anesthesia is necessary; there is no danger of shock or hemorrhage, and no local infection can follow the procedure. Usually no pain is produced by treatment; no impairment of hearing or disability follows, and, finally, treatment can be instituted even in the presence of cardiac or pulmonary pathologic conditions. It is felt that only the tissue that functions poorly if at all is destroyed.

During the past five or six years the effects of roentgen therapy on several hundred patients with enlarged tonsils, adenoid tissues and cervical glands have been observed. Selection of patients is important, and experience has shown the type of infection that responds to roentgen therapy. Soft tonsils with open crypts respond better than hard, firm tonsils with crypts that have only small pinhead openings that do not facilitate free drainage. The crypts extending to the base of such tonsils may be just as large, but their external openings are very small; these tonsils do not respond so well to irradiation. The most favorable group of patients consists of children 1 to 6 years of age in whom obstruction of the nasopharynx is not too great. In children aged 1 to 4, the results are often not short of miraculous. Those who snore at night, owing to obstruction, often get relief after one or two treatments. Those with repeated infections, often associated with enlarged cervical glands, are also greatly benefited. Children who have had

tonsillitis recurring every two to four weeks often go for one or more years without a recurrence. Improvement in health is comparable to that following tonsillectomy, without any of the after-effects. Various disturbances caused by focal infection gradually subside.

Irradiation therapy can be given any time after remission of the acute infection, whereas sometimes several months must elapse before the patient's health would justify tonsillectomy. It is the consensus that tonsillectomies should not be performed during any period when infantile paralysis is prevalent, yet there are many children who seek relief from their symptoms. Allergic persons may be tided over by irradiation, and in many cases the improvement following irradiation is so decided that operation may not be necessary. Irradiation may be performed in the presence of severe cardiac or pulmonary disease, diabetes or hemophilia and in cases in which anesthesia would be dangerous or the physical condition of the child precludes operation.

In my practice a record of the acute infections of the throat in the winter of 1943-1944 revealed as many severe infections in children who had had tonsils removed as in those whose tonsils were still present, and a lower incidence of infections of the throat in those properly selected patients whose tonsils had been irradiated. Pathologic examination of several tonsils that had been previously irradiated showed no unusual changes in the lymphoid structure, and the operative removal of these tonsils was not more difficult. It was noted that some of these children seemed to have a speedier convalescence than those who had not had previous roentgen therapy.

In summary, roentgen treatment of hypertrophied tonsils and adenoids is not advised as the only method of treating the enlarged lymphoid tissue in the throat, but it should be considered in selected cases before one resorts to surgical intervention, especially when there are contraindications to surgical treatment. The results of irradiation in the past were often disappointing, principally because of improper selection of cases and inadequate application of the roentgen treatment. Further experience with this method will undoubtedly justify its more frequent use.

Rhinopharyngeal Aspects. SAMUEL J. PEARLMAN.

The chief reason for removal of the tonsils is the occurrence of frequent, more or less severe attacks of tonsillitis, peritonsillitis and peritonsillar abscess. Were this indication closely adhered to, there would be little cause for complaint. If tonsils are cleanly removed, there can be no more attacks of tonsillitis, although this does not mean that there cannot be more attacks of sore throat, for these do happen, sometimes more frequently than before operation. All other reasons for removal of the tonsils are less important, and the more often tonsils are removed for these lesser reasons the more often will disappointment be encountered.

Acute, recurrent attacks of cervical adenitis occurring with bouts of tonsillitis and chronic enlargement of lymph nodes in the anterior triangles of the neck, reasonably thought to be due to diseased tonsils, are the next best reason for tonsillectomy. There will be a high percentage of improvement following operation, but the glands will not always disappear rapidly and in a fair percentage of cases will continue to be the seat of acute and recurring attacks of inflammation.

Another reason for advising removal of the tonsils is their enlargement. Instances in which the tonsils are so large as to interfere with deglutition or breathing are infrequent, and it is my feeling that in most cases simple enlargement is not adequate justification for surgical removal.

Another common cause for recommendation of tonsillectomy is the theory that the tonsils are the seat of infection transmitted to other parts of the body and resulting in arthritic phenomena, generalized muscular aches and pains, neuritis, endocarditis, nephritis and other manifestations. The fact that the tonsils are or may be such a focus is evident, but the many instances of failure of tonsillectomy to remedy ailments already present and to prevent their occurrence justify revision of the positiveness with which the tonsils are accused of being the cause

and warrant the use of measures less extreme. In a large group of lesser ailments little or no benefit may be expected from operation. There is no reason to believe that tonsillectomy can be of value in cases of lack of appetite and failure to gain weight, which may often be due to constitutional and hereditary causes.

The best reason for adenoidectomy is the presence of an amount of lymphoid tissue in the nasopharynx so large as to interfere seriously with nasal breathing. In this situation the more gratifying results are obtained after proper operation. In those cases in which the adenoids alone are at fault, the surgeon should be courageous enough to advocate their removal only, with sparing of the tonsils. It may be pointed out that, instead of removal of the tonsils being given more than its share of credit, much of the credit for the benefits following the combined operation should be properly assigned solely to romoval of the adenoids.

In handling diseases of the tonsils and adenoids, there is no one perfect method. There are adequate reasons for surgical removal of these structures, but, as elsewhere in the body, a surgical procedure should not be carried out without proper indications. When tonsils alone are diseased, they alone should be removed. When adenoids alone are at fault, they should be handled separately. When there is much lymphoid hypertrophy in the pharynx, which causes trouble before operation or difficulties after operation, the parents should be told that there are methods of handling other than surgical intervention, such as roentgen therapy before, after or in combination with surgical procedure. When age, some other illness, the presence of an epidemic or the absence of clearcut indications for surgical intervention makes an operation undesirable for the time being, this is a safe and efficient procedure. At all times the pediatrician should be the guide. The care of the child with diseased tonsils and adenoids is a problem for the pediatrician, the laryngologist and the radiologist, working in conjunction, if the patient is to receive maximum benefit.

Roentgen Aspects. ERICH M. UHLMANN.

In planning irradiation therapy the radiologist is influenced mainly by three considerations: (1) the indication for irradiation, (2) the proper timing and (3) the method of application. The best technic will be of little value if not properly integrated with the general plan of therapy, and the method of treatment must be subjected to critical clinical observation and experience. For this reason the technical execution of irradiation therapy frequently undergoes changes depending on the evaluation of clinical results. I believe that the simplest, as well as the safest, method of administration for the conditions in question is the external application of roentgen rays. During the past seven years in the Tumor Clinic of Michael Reese Hospital, more than 1,000 patients have received roentgen therapy for recurrent colds, infections of the throat, cervical lymphadenopathy, impaired hearing and other symptoms associated with enlargement of the tonsils or with the existence of hypertrophic lymphoid tissue in the pharynx.

Under proper supervision the method described is without danger and requires not more than three visits to an institution with facilities for administering roentgen therapy. No special equipment is necessary, nor are any particular ill effects to be anticipated. I believe that my experience justifies recommendation of this form of therapy for the described pathologic conditions, if there is no definite indication for surgical intervention.

During the period from February 1938 until the end of December 1942, almost 600 patients were treated, 480 of whom could be traced and checked satisfactorily. In order to evaluate the results the patients have been classified into five groups.

Group 1 includes 120 persons (25 per cent of the total) who had complete cessation of all symptoms for which treatment was given. Of the 120, 72 (60 per cent) had cervical lymphadenopathy in addition to hypertrophic lymphoid tissue in the pharynx, and 10 patients (8.3 per cent) also suffered from impaired hearing. Twenty-eight patients (23.3 per cent) had undergone tonsillectomy prior to irradiation therapy without more than temporary benefit. In the group of 120 were

patients who had had recurrent attacks of fever, often six to nine times during one year, associated with infected and enlarged tonsils, difficulty in breathing, cervical lymphadenopathy, pain on swallowing, headaches and general malaise. All these symptoms cleared up promptly following treatment and did not recur during the observation time. There are also in this group children who felt permanently below par and whose parents complained of their lack of appetite and failure to gain weight. These children showed improvement of the objective symptoms and started to gain weight within a short time.

It is interesting to note that 3 of the 120 patients (2.5 per cent) underwent tonsillectomy subsequent to roentgen therapy, and an analysis of their histories shows that this procedure was not warranted.

Group 2, a total of 216 patients (45 per cent of the entire group of 480), comprises those who showed considerable improvement but occasionally experienced minor symptoms. Of this group, 152 (approximately 70 per cent) were under 10 years of age. Of the total, 108 (50 per cent) had cervical lymphadenopathy, and 12 (5.5 per cent) suffered from impaired hearing. Thirty-four (15.7 per cent) had undergone tonsillectomy without appreciable benefit; 18 (8.3 per cent) had tonsillectomy at various times following irradiation therapy, and on 50 per cent operation was performed without specific indications. The response of this group was not so dramatic as that of group 1. Included are some patients who received a second course of therapy between two and four years after the original course and thereafter had complete cessation of all previous symptoms.

In group 3, a total of 80 patients (16.6 per cent), only temporary improvement followed irradiation therapy. Symptoms recurred after several months of well-being, usually less severe and often not considered of sufficient importance to warrant resumption of therapy. Sixty-eight (85 per cent) of this group were under 10 years of age. Forty patients (50 per cent) had cervical lymphadenopathy, and 7 (8.7 per cent) had impaired hearing. Nine patients (11.2 per cent) had had tonsillectomy prior to irradiation and 29 (36.2 per cent) subsequent to therapy. In this group is included a large number of patients with allergic conditions who had definite improvement after irradiation but who suffered from symptoms attributed to the allergic condition rather than to the organic changes. There were permanent contraindications to surgical procedure in some of the patients who failed to receive complete benefit and in others the improvement of the condition was sufficient to eliminate further expectation of benefit from surgical intervention.

Group 4, 57 patients (11.9 per cent), showed no appreciable improvement following therapy. In this group 50 (87 per cent) were under 10 years of age; 23 (40 per cent) had cervical lymphadenopathy, and 6 (10.5 per cent) had impaired hearing. Fourteen (24.5 per cent) had undergone tonsillectomy prior to irradiation therapy and 13 (22.8 per cent) afterward. There were valid reasons why surgical treatment was not considered for the majority of these patients; many had heart failure or kidney disease or were highly allergic.

Group 5, the last group, consisted of 7 patients (1.5 per cent), a number too small for statistical evaluation. In this group the condition was worse after therapy than it had been before. However, in no instance did the change for the worse occur immediately following treatment or was it considered to be due to the therapy. These patients did not present themselves with especially severe symptoms. One patient underwent tonsillectomy before irradiation, and in 4 tonsillectomies were performed after treatment; only 1 of the 4 had definite improvement from tonsillectomy.

In analyzing these results, certain conclusions are drawn. Of the total of 480 patients, 42 per cent were less than 5 years of age and 76 per cent less than 10 years of age. Since in this age group the chances for spontaneous improvement without therapy are much less than in the group from 10 to 15 years of age and since improvement was considered due to irradiation therapy only when the change took place within a reasonable time (four to six weeks) following treatments, I believe the factor of spontaneous improvement did not materially influence the results.

It must be emphasized that many of those patients in whom irradiation therapy proved a complete failure offered poor prospects for any form of therapy, inasmuch as they included those suffering from a status allergicus, with hay fever, asthma, cutaneous diseases and other symptoms. For more than 50 per cent of them surgical procedures were never considered.

DISCUSSION

DR. MORLEY D. MCNEAL: I should like to ask Dr. Pearlman if the previous roentgen treatment created any difficulty for tonsillectomy if this was done later.

DR. JOHN L. REICHERT: Has Dr. Rosenblum ever found that in children in whom the respiratory allergy was outstanding this was aggravated by irradiation as it is sometimes by surgical removal of tonsils and adenoids?

DR. THEODORE J. WACHOWSKI: I should like to ask Dr. Pearlman what the incidence of sinus infection was in this series and also to ask Dr. Uhlmann whether he used the beam of roentgen rays over the paranasal sinuses or whether he drew a line rather sharply as to selection of the area treated.

DR. PHILIP ROSENBLUM: Allergic children often have simple hypertrophy of the tonsils from infancy. As a group, these children respond well to irradiation, without having to experience any of the dangers often associated with operative procedures and anesthesia of which they are sometimes victims.

DR. SAMUEL J. PEARLMAN: In answer to Dr. McNeal, in my experience the use of irradiation prior to tonsillectomy did not make any particular difference later, when operation was found to be necessary.

I have no figures as to those who had sinusitis. If the question means "Was there improvement of sinusitis after treatment?" my impression is that there was. Many times when we used irradiation it was given over the sinuses when involved, as well as directed toward the tonsils and adenoids.

DR. ERICH M. UHLMANN: There were a few patients who suffered from sinusitis in addition to pathologic changes in the tonsils and adenoids. However, patients whose symptoms were localized predominantly in the sinuses were excluded from this survey. Their response to therapy will be analyzed in a separate study. Roentgen therapy for sinusitis was given under entirely different technical conditions.

Louis W. Sauer, M.D., *President*

Stanley Gibson, M.D., *Physician-in-Chief, Children's Memorial Hospital, Presiding*

Feb. 19, 1946

The clinical presentations were given by members of the Children's Memorial Hospital staff. The meeting was held at this hospital.

Patent Ductus Arteriosus with Superimposed Staphylococcus Aureus Endarteritis. DR. JOHN F. DAMMANN JR.

L. P., a white girl aged 9, entered the hospital with an eighteen day history of high fever, loss of weight, severe cough, anorexia and vomiting. A cardiac murmur was noted at the age of 1; she had never gained weight properly and had never been able to engage in active exercise because of dyspnea on exertion.

Physical examination revealed an acutely ill, underweight, dehydrated child with a temperature of 105.6 F. and rapid, grunting respirations. There were fine and medium rales throughout the chest, most noticeable at the base of the left lung. There was dulness at the bases of both lungs. The heart was enlarged to percussion. There was a strong basal systolic thrill and a typical machinery

murmur best heard in the second interspace of the ribs on the left side. A capillary pulse was present, and the blood pressure was 125 systolic, 60 diastolic. Both spleen and liver were enlarged.

A roentgenogram of the chest showed consolidation in the lower axillary region on the left side and some increase in markings in both hilar regions. The heart was enlarged 20 per cent, and the pulmonary cone was moderately prominent. An electrocardiogram showed a tendency toward left axis deviation. Results of examinations of the blood and urine were essentially normal. Three blood cultures were positive for Staphylococcus aureus.

A diagnosis of patent ductus arteriosus, with a superimposed bacterial endarteritis with emboli lodging in the lung, was made. Therapy with penicillin and sulfathiazole was instituted and carried on for a twenty-five day period, during which the patient showed improvement, as proved both by clinical examination and by laboratory data. Therapy was discontinued, and she was watched for one month without showing signs of return of the endarteritis. She was then sent to Dr. Van Hazel at St. Luke's Hospital, where surgical ligation of the patent ductus arteriosus was performed. Her postoperative course was uneventful.

At present, a year following the acute episode, she appears to be a healthy child. Her heart is now normal. The blood pressure is 112 systolic, 74 diastolic. She has shown no signs of recurrence of the endarteritis. Her exercise tolerance has increased, and gain in weight has been normal.

Coarctation of the Aorta, with Superimposed Bacterial Endarteritis. DR. C. R. LEININGER.

J. D., a white boy aged 10 years, was admitted to the hospital with a sudden onset of fever and pain and a limp in the right leg. The referring diagnosis was early poliomyelitis or acute rheumatic fever. The previous medical history was noncontributory. The temperature on admission was 105 F. On physical examination the child was seen to be oriented but irritable, with a slightly enlarged heart and a basal and suprasternal systolic thrill and murmur transmitted into the neck, especially on the right side. The blood pressure in each arm was 120 systolic, 75 diastolic; in each leg it was 50 systolic, diastolic undetermined. Pulsations in the femoral arteries were barely perceptible. A roentgenogram of the chest revealed a narrow upper mediastinum, a 20 per cent cardiac enlargement and no erosion of the ribs.

The patient had a septic course for six days; then he had a normal temperature until discharge from the hospital. At the time of admission he had complained of pain and had had a definite tenderness over the lateral aspect of the right foot. The skin over this area gradually became discolored and then regressed. The spleen was palpable during the first week of illness. Two blood cultures taken during spiking fever yielded hemolytic Staph. aureus.

A diagnosis of coarctation of the aorta with acute bacterial endarteritis was made. Sulfadiazine and 240,000 units of penicillin daily were prescribed. After 5,000,000 units of penicillin had been given, four consecutive blood cultures failed to reveal the organisms. The patient was discharged on the forty-third hospital day.

He was followed in the outpatient department and was asymptomatic until Feb. 11, 1946, when he was readmitted to the hospital, with a history of pain in the left leg, fever and headache. Physical symptoms were unchanged except for mild tenderness in the calf of the left leg, which subsided promptly. He has had an intermittent fever. Three blood cultures have shown Streptococcus viridans.

In reviewing the literature to find other similar cases of endarteritis caused by Staph. aureus, we found only 1 case, reported by Touroff, of a patent ductus arteriosus. We have been unable to find another case of coarctation of the aorta with a superimposed endarteritis due to Staph. aureus.

Malrotation of the Colon with Volvulus. DR. ELMER STERNBERG.

G. R., a 3 month old white boy, entered the hospital with a complaint of intermittent vomiting since birth. The first attack occurred in the hospital shortly

after delivery. There he was considered to be a feeding problem. At home he continued to vomit every second or third feeding. The vomitus was bile stained. The stools were yellow-green and of normal consistency. On the twelfth day of life, Similac[1] was prescribed. The vomiting ceased, and the child was well for five weeks. At 7 weeks of age and again at 12 weeks, he had mild attacks of vomiting and diarrhea. The vomiting was projectile. The attacks lasted two days. At 12 weeks of age, four days prior to admission here, he began to have severe, projectile vomiting. Very little was retained. The vomitus was always bile stained. Stools were loose, and he had a low grade fever. At another hospital studies were made with barium sulfate and were reported on as showing prolonged gastric emptying time. He entered our hospital for a more complete work-up.

Physical examination revealed a well developed, undernourished, dehydrated infant weighing 9 pounds 2½ ounces (4,153 Gm.). He did not appear acutely ill. His temperature was normal. Physical examination showed nothing significant except a distended abdomen. No abdominal masses were felt. The liver, kidneys and spleen were not palpable. No pyloric tumor could be felt, and no peristaltic waves were seen. Routine laboratory studies yielded negative results. The conditions considered here were (1) atypical pyloric stenosis, (2) congenital stenosis of the intestine or (3) intestinal obstruction. Review of the roentgenograms revealed a high grade obstruction of the duodenum at the junction of the third and fourth portions. The duodenum was greatly dilated, with very little barium passing into the small intestine. The stomach was normal. In view of the history and physical and roentgen observations, a preoperative diagnosis of duodenal obstruction due to malrotation of the colon was made.

An exploratory laparotomy on the second hospital day revealed a volvulus of the small intestine and malrotation of the colon, with a peritoneal fold compressing and obstructing the duodenum. The volvulus was relieved; the peritoneal fold was incised, which relieved the obstruction, and the colon was reflected to the left side of the abdomen. Routine closure of the abdominal layers was done.

Postoperative care consisted of administration of parenteral fluids, transfusion of whole blood and a postpyloric feeding regimen started twelve hours postoperatively. The course was uneventful until the eighth postoperative day, when evisceration occurred while the skin sutures were being removed. The wound was repaired with the patient under general anesthesia. At this time the colon was seen to lie in the left side of the abdomen where it had been placed during the original operation. The postoperative care was essentially the same with the addition of penicillin and of subcutaneously administered sulfadiazine. The patient had an elevation of temperature to 103 F. for two days, after which it dropped to normal and remained so. Postpyloric feedings were increased gradually until he was taking 5 ounces (150 cc.) of evaporated milk every four hours and retaining it. Sutures were removed on the tenth and fifteenth days postoperatively. The wound was well healed, and the patient was discharged on the twenty-seventh hospital day. He weighed 8 pounds 12 ounces (3,969 Gm.).

He returned six weeks after discharge for roentgen studies to determine the position of the bowel. A barium sulfate enema revealed the descending and transverse colon to be entirely to the left of the spine. The child was doing well and had gained almost 4 pounds (1,814 Gm.) since discharge.

Micrognathia. DR. WILLIAM Y. TAKAHASHI.

M. P., a 2 week old boy, was admitted to the hospital with the chief complaints of not feeding well and of difficulty in breathing. He was cyanotic at birth and had frequent episodes of intense dyspnea and cyanosis, especially during feeding.

1. According to the manufacturer, Similac is a powdered modified milk product made from tuberculin-tested cow's milk (with the casein modified) from which part of the butter fat is removed and to which are added lactose, olive oil, coconut oil, corn oil and a fish liver oil concentrate.

His respirations were usually labored and irregular but were relieved somewhat by placing him on his side. Sometimes respiration stopped entirely, the infant requiring artificial resuscitation. He was unable to use the nipple and had to be fed with a syringe. At times he regurgitated through the mouth and nose.

On examination he presented multiple congenital anomalies. Most striking was the small, receding chin. This condition contributed to the dropping back of the tongue into the pharynx, producing respiratory obstruction. In addition, there were complete cleft palate, mild flexion contracture of the elbows, spade hands, bowing of the tibias, talipes equinovarus and clawfeet.

In the hospital, the Breck feeder proved the most satisfactory of the methods of feeding tried. A suture was placed in the tongue to relieve dyspnea by pulling on it as needed. Gradually respiration became more normal, and the patient gained weight.

(The embryologic development of the mandible was reviewed. The etiology of micrognathia is undetermined, but various theories, notably the hereditary factor, the possibility of prenatal nutritional deficiency and the question of pressure on the mandible during fetal growth, were considered. It was felt that, when possible, simple methods rather than mechanical and surgical means were preferable in relieving dyspnea.)

Pleural Effusion. DR. HARRY FARRELL.

C. C., a boy aged 12, was admitted to the hospital on Jan. 23, 1946, with severe pain in the right side of the chest on respiration, which had begun suddenly and was preceded only by a mild cold. There was a history of a ruptured appendix and of peritonitis four months previously.

Examination revealed a distressed, slightly cyanotic, acutely ill boy with a temperature of 104 F. There was decreased expansion of the right side of the chest on respiration, with decreased to absent breath sounds and dulness to flatness inferiorly on the right. The heart was not displaced. No abdominal mass or tenderness was ascertained, and the liver was at the costal border. An appendectomy scar existed in the right lower quadrant of the abdomen.

Roentgen examination showed much fluid at the base of the right lung, with extension to a lesser degree almost to the apex and evidence of some loculation. Thoracocentesis revealed serosanguinous sterile fluid, with many polymorphonuclear cells. Penicillin was injected into the pleural cavity. A second tap was done about ten days later, revealing clear, yellow, sterile fluid. The white blood cell count was 9,650, with 84 per cent polymorphonuclear leukocytes. The Mantoux test elicited a positive reaction.

The patient's temperature spiked daily to 104 F., but after a few days it began gradually to subside, and it is now below 100 F. Therapy with penicillin and sulfonamide compounds was stopped because of sensitivity, without affecting his course.

This patient has presented an interesting diagnostic problem. In the first place, the question has arisen as to whether the chest condition is secondary to a subphrenic abscess complicating the previous peritonitis. Inasmuch as the reaction to the Mantoux test is positive, a tuberculous pleurisy must be considered. The third possibility is an atypical pleurisy with effusion, resulting from pneumonia. These questions have not yet been answered.

The following cases, which were presented, are being submitted for publication:

Kaposi's Disease: Report of Two Cases. DR. BRUCE NEWMAN.

Mirror Movements. DR. CAROL SMITH.

Enterogenous Cyst of the Ileocecal Region. DR. WILLIAM J. MORROW, with DR. W. HARRISON MEHN.

Congenital Porphyria: Report of a Case. DR. IRVIN DUNSKY.

Book Reviews

Physical Chemistry of Cells and Tissues. By Rudolf Höber, with the Collaboration of David I. Hitchcock, Ph.D.; J. B. Bateman, Ph.D.; David R. Goddard, Ph.D., and Wallace O. Fenn, Ph.D. Price, $9.00. Pp. 676, with 70 illustrations. Philadelphia: The Blakiston Company, 1945.

This is an excellent book for the specialist in the field of biophysical chemistry. The first section, of 90 odd pages, by Hitchcock, covers all of the fundamentals, such as diffusion in liquids, reaction velocity and enzyme action, elements of thermodynamics, electromotive force and properties of aqueous solutions, all stated in highly technical terminology but with little effort to interpret the significance of these phenomena in common terms for the reader who has a legitimate interest but lacks the technical training of the specialist.

The second section, of 120 pages, by Bateman, deals with large molecules and is much more readable. The third, fourth and fifth sections, by Höber, covering 138 pages, all deal with protoplasm, both mechanistically and as a living system, and are readily comprehensible by any one with minimum basic training.

The sixth section, by Goddard, covers phenomena of respiration in a manner in line with the most advanced concepts of today, with a great deal of highly technical exposition, much of which will be meaningless to the less informed reader but indispensable, nevertheless, for complete understanding of cellular respiration.

Section seven, by Fenn, deals with the contractile process in all its variations. This is the first general review of muscle which takes into account the potential significance of the more recent work on the function of myosin in the energy cycle.

The eighth section, by Höber, deals with passive penetration and active transfer in both animal and plant tissues and covers such problems as intestinal absorption, formation of urine, elaboration of digestive juices, permeability of body surfaces and the mechanisms involved. There is nothing particularly new, although the review of literature is well up to date and generally readable. The book is a "must" for the reference library, apparently being designed exclusively for the researcher. This reviewer, however, feels that such works would be infinitely more valuable and effective if the authors would take a little more pain to interpret the subject matter in simplified text as a supplement to the highly technical material. Such a format need sacrifice neither scientific accuracy nor technical formulas but could carry the authors' theses to a worthy group of collaborators, such as the physician specialists, who have not had an opportunity to become physical chemists as well.

This volume is a remarkable condensation of information into a small space.

Hematology for Students and Practitioners. By Willis M. Fowler, M.D. Price, $8.00. Pp. 499, with 110 figures and 8 colored plates. New York: Paul B. Hoeber, Inc. (Medical Book Department of Harper & Brothers), 1945.

This is a complete textbook on hematology written from the viewpoint that hematology is a part of internal medicine rather than a specialty. It therefore contains much of clinical interest, and controversial questions that would be of interest only to the specialist have been kept at a minimum. It contains a chapter on "Whole Blood and Blood Derivatives" by Elmer L. DeGowin, M.D., which should be of particular interest to the returning medical officer.

The bibliography is adequate and, being contained at the end of each chapter, does not clutter up the text. This should be an interesting volume for the student or practitioner.

Directory of Pediatric Societies *

INTERNATIONAL

International Association of Preventive Pediatrics

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Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

International Congress of Pediatrics

President: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
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Canadian Committee:
Chairman: Dr. Alan Brown, Hospital for Sick Children, 67 College St., Toronto 2.
Secretary: Dr. H. P. Wright, 1414 Drummond St., Montreal.
Place: New York. Time: Sept. 16-19, 1947.

International Congress for the Protection of Infancy

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.

Save the Children International Union

President: Mrs. Gordon Morier.
Secretary: Dr. Georges Thélin, 43 Quai Wilson, Geneva, Switzerland.
Place: Geneva, Switzerland, Time. Sept. 17-20, 1946.

FOREIGN

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Associação Paulista de Medicina, Seccaõ de Pediatrias

President: Dr. Vicente Lara.
First Secretary: Dr. Armando de Arruda Sampaio.
Second Secretary: Dr. Luiz Augusto Monteiro Toledo, Av. Brigadeiro Luiz Antonio 393, 1° Andar, São Paulo, Brazil.
Time: Twelfth of every month, 8:30 p. m.

British Paediatric Association

President: Prof. G. B. Fleming, 13 Lynedoch Crescent, Glasgow.
Joint Secretary: Prof. Alan Moncrieff and Dr. Donald Paterson, Hospital for Sick Children, Great Ormond St., London, W. 1.
Place: Rugby School, Rugby. Time: Aug. 1-3, 1946.

Danish Pediatric Society

President: Dr. E. Lenstrup, Copenhagen.
Secretary: Dr. Gjørup, Dronning Louises Børnehospital, Copenhagen.

Nederlandische Vereeniging voor Kindergeneeskunde

President: Dr. J. H. G. Carstens, Servaas Bolwerk 14, Utrecht.
Secretary: Dr. R. P. van de Kasteele, Lyccumplein 10, den Haag.
Place: Children's Hospital or Pediatric Clinic. Time: Three times a year.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

PALESTINE JEWISH MEDICAL ASSOCIATION, SECTION OF PHYSICIANS OF CHILDREN'S DISEASES

President: Prof. L. F. Meyer, 29 Toelsohn St., Tel Aviv.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv.

ROYAL SOCIETY OF MEDICINE, SECTION FOR THE STUDY OF DISEASE IN CHILDREN

President: Prof. Norman Capon, 49A Rodney St., Liverpool, England.
Secretary: Dr. J. N. O'Reilly, 46 Harley St., London, W. 1, England.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:15 p. m.

SOCIEDAD CUBANA DE PEDIATRIA

President: Dr. Teodosio Valledor, Habana.
Secretary: Dr. Carlos Hernandez Miyares, Hospital Nuestra Señora de las Mercedes L y 21, Apartado, 2430, Habana.
Place: Cátedra de Clinica Infantil, Hospital Nuestra Señora de las Mercedas y Hospital Municipal de Infancia, Habana. Time: Last Wednesday of every month.

SOCIEDAD ECUADORIANA DE PEDIATRIA

President: Dr. Francisco de Icaza Bustamente.
Secretary: Dr. M. I. Gómez Lince, P. O. Box 693, Guayaquil.

SOCIEDAD MEXICANA DE PEDIATRIA

President: Dr. Fernando López Clares, 12/a. Medellín 191, Mexico.
Secretary: Dr. Jesus Gómez Pagola, Versalles 64, Mexico.

SOCIEDAD DE PEDIATRIA DE CÓRDOBA

President: Dr. Juan Francisco Herrera, Córdoba, Argentina.
Secretary: Dr. Bernardo Serebrinsky, Dean Funes 2000, Esq. Ocaña (N.), Córdoba. Argentina.
Place: Comite pro Defenso del Niño, Dean Funes 2000, Córdoba, Argentina. Time: Once a month.

SOCIEDAD DE PEDIATRÍA DE SANTIAGO DE CUBA

President: Dr. Antonio Béguez César, Sagarra 107, Santiago de Cuba.
Secretary: Dra. Susana Texdó Vaillant, Padre Pico 57, Santiago de Cuba.
Place: Colegio Médico. Time: Last Tuesday of every month.

SOCIEDAD VENEZOLANA DE PUERICULTURA Y PEDIATRIA

President: Dr. Pedro J. Alvarez.
Secretary: Dr. Ernesto R. Figueroa, 3a Avenida 10, Bella Vista, Caracas.
Place: Hospital Municipal de Niños Jose Manuel de los Rios, Caracas.

SOCIÉTÉ DE PÉDIATRIE DE PARIS

President: Dr. Leveuf, Paris, France.
Secretary: Dr. Jean Hallé, 10 bis Rue Pré aux Clercs, Paris, France.
Place: Hôpital des Enfants Maladies, 149 Rue de Sèvres. Time: 4:30 p. m., third Thursday of every month.

SWEDISH MEDICAL SOCIETY, SECTION FOR PEDIATRICS AND SCHOOL HYGIENE

President: Prof. Arvid Wallgren, 53 Strandvägen, Stockholm.
Secretary: Dr. Henning Magnusson, 58 Odengatan, Stockholm.
Place: Various clinics and hospitals in Stockholm and Uppsala. Time: Second Friday of each month (except summer).

URUGUAYAN SOCIETY OF PEDIATRICS

President: Dr. Jose Bonaba, Montevideo.
Secretary: Dr. Héctor Fossatti, Durazno 1882, Montevideo.
Place: Club Medico del Uruguay, Avenida Agraciado 1464 (Piso 13), Montevideo

NATIONAL

American Medical Association, Scientific Assembly, Section on Pediatrics

Chairman: Dr. John Aikman, 184 Alexander St., Rochester, N. Y.
Secretary: Dr. Gilbert J. Levy, 188 S. Bellevue Blvd., Memphis, Tenn.

American Academy of Pediatrics

President: Dr. Jay I. Durand, 515 Cobb Bldg., Seattle, Wash.
Secretary: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.
Place: Hotel William Penn, Pittsburgh. Time: Nov. 13-16, 1946.

American Hospital Association, Massachusetts Hospital Association

Chairman: Dr. Frank Wing, Boston.
Secretary: Dr. W. Franklin Wood, McLean Hospital, Waverly 79, Mass.
Place: Boston. Time: November 1946.

American Pediatric Society

President: Dr. Harold K. Faber, 2361 Clay St., San Francisco.
Secretary-Treasurer: Dr. Henry G. Poncher, 1819 W. Polk St., Chicago 12.

Canadian Society for the Study of Diseases of Children

President: Dr. H. S. Little, 300 Dufferin Ave., London, Ontario.
Secretary-Treasurer: Dr. Elizabeth Chant Robertson, 67 College St., Toronto 2.
Place: Banff, Alberta. Time: June 14-15, 1946.

Society for Pediatric Research

President: Dr. Mitchell I. Rubin, 219 Bryant St., Buffalo 9, N. Y.
Secretary: Dr. Robert F. Ward, Bellevue Hospital, New York 16.

SECTIONAL

Intermountain Pediatric Society

President: Dr. Robert Alway, University of Utah School of Medicine, Salt Lake City 2.
Secretary-Treasurer: Dr. L. Paul Rasmussen, 1020 Boston Bldg., Salt Lake City 1.
Place: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

New England Pediatric Society

President: Dr. James Marvin Baty, 1101 Beacon St., Brookline, Mass.
Secretary-Treasurer: Dr. Charles D. May, 300 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Three meetings a year, occurring from September to May.

North Pacific Pediatric Society

President: Dr. Percy Guy, 502–2d Ave., Seattle, Wash.
Secretary: Dr. Aldis B. Johnson, 515 Cobb Bldg., Seattle, Wash.
Place: Vancouver, B. C. Time: Oct. 19, 1946.

Northwestern Pediatric Society

President: Dr. George B. Logan, 102 Second Ave. S. W., Rochester, Minn.
Secretary-Treasurer: Dr. Northrop Beach, 1009 Nicollet Ave., Minneapolis.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. G. R. Fisher, 23 E. Pikes Peak Ave., Colorado Springs, Colo.
Secretary: Dr. Joseph H. Lyday, 1850 Gilpin St., Denver 2.

SOUTHERN MEDICAL ASSOCIATION, SECTION OF PEDIATRICS

Chairman: Dr. William Weston Jr., 1428 Lady St., Columbia, S. C.
Secretary: Dr. Angus McBryde, 604 W. Chapel Hill St., Durham, N. C.

STATE

ALABAMA PEDIATRIC SOCIETY

President: Dr. Jerome C. Chapman, 2160 Highland Ave., Birmingham.
Secretary-Treasurer: Dr. Ruth Berrey, 2021–6th Ave. N., Birmingham.
Place: Birmingham. Time: September 1946.

ARIZONA PEDIATRIC SOCIETY

President: Dr. W. P. Sherrill, 342 W. McDowell Rd., Phoenix.
Secretary: Dr. W. F. Schoffman, 926 E. McDowell Rd., Phoenix.
Place: Phoenix or Tucson. Time: At time of state meeting.

ARKANSAS STATE PEDIATRIC ASSOCIATION

Chairman: Dr. C. B. Billingsley, 1425 N. 11th St., Fort Smith.
Secretary: Dr. R. E. Weddington, 1425 N. 11th St., Fort Smith.

CALIFORNIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

Chairman: Dr. Charles W. Leach, 2000 Van Ness Ave., San Francisco 9.
Secretary: Dr. Chester I. Mead, 1930 Truxton Ave., Bakersfield.
Place: Biltmore Hotel, Los Angeles. Time: May 7-10, 1946.

FLORIDA STATE PEDIATRIC SOCIETY

President: Dr. Councill Rudolph, 103–5th St. S., St. Petersburg.
Secretary: Dr. Robert Blessing, 409 Blount Bldg., Ft. Lauderdale.
Place: Concurrent with state association convention and fall meeting.

GEORGIA PEDIATRIC SOCIETY

President: Dr. Alton Johnson, 102 E. Central Ave., Valdosta.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.
Place: Atlanta. Time: At time of annual state meeting.

HEZEKIAH BEARDSLEY PEDIATRIC CLUB OF CONNECTICUT

President: Dr. Edward T. Wakeman, 129 Whitney Ave., New Haven.
Secretary: Dr. Herman Yannet, Southbury Training School, Southbury.
Place: New Haven. Time: September 1946.

ILLINOIS STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

Chairman: Dr. Craig D. Butler, 715 Lake St., Oak Park.
Secretary: Dr. A. J. Fletcher, 139 N. Vermilion, Danville.

INDIANA STATE PEDIATRIC SOCIETY

President: Dr. K. T. Knode, 1105 E. Jefferson Bldg., South Bend.
Secretary-Treasurer: Dr. Matthew Winters, 621 Hume Mansur Bldg., Indianapolis.
Time: Two meetings a year.

IOWA PEDIATRIC SOCIETY

President: Dr. Arnold M. Smythe, 406–6th Ave., Des Moines.
Secretary-Treasurer: Dr. James Dunn, 414 Blackhawk Hotel, Davenport.
Place: Des Moines. Time: April 18, 1946.

Louisiana State Pediatric Society

President: Dr. S. George Wolfe, 1560 Line Ave., Shreveport.
Secretary-Treasurer: Dr. W. C. Rivenbark, 1448 Louisiana Ave., New Orleans 15.

Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. Carl H. Laws, 12 Pierrepont St., Brooklyn, N. Y.
Secretary: Dr. George R. Murphy, 292 Madison Ave., New York.
Place: Hotel Pennsylvania, New York. Time: May 2-3, 1946.

Medical Society of the State of Pennsylvania, Pediatric Section

Chairman: Dr. Elwood W. Stitzel, 403 Central Trust Bldg., Altoona, Pa.
Secretary: Dr. P. F. Lucchesi, Philadelphia Hospital, Philadelphia.

Michigan State Medical Society, Pediatric Section

Chairman: Dr. Donald J. Barnes, 3001 W. Grand Blvd., Detroit, Mich.
Secretary: Dr. Mark F. Osterlin, Central Michigan Children's Clinic, Traverse City.
Place: Detroit. Time: Sept. 25-27, 1945.

Mississippi State Pediatric Society

President: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Secretary: Dr. Guy Verner, 126 N. Congress St., Jackson.

Nebraska Pediatric Society

President: Dr. John M. Thomas, 1418 Medical Arts Bldg., Omaha 2.
Secretary-Treasurer: Dr. Gerald C. O'Neil, 640 City National Bank Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

New Mexico State Pediatric Society

President: Dr. M. K. Wylder, 221 W. Central Ave., Albuquerque.
Secretary-Treasurer: Dr. Ly Werner, 221 W. Central Ave., Albuquerque.

North Carolina Pediatric Society

President: Dr. Charles R. Bugg, Professional Bldg., Raleigh.
Secretary: Dr. Charles F. Williams, 817 Hillsboro St., Raleigh.
Place: Roaring Gap. Time: September 1946.

Northern California Pediatric Society

President: Dr. Edith M. Meyers, 431–30th St., Oakland.
Secretary: Dr. A. L. Gleason, 411–29th St., Oakland 9.
Place: San Francisco. Time: Second Thursday of February, April, September and November.

Oklahoma State Pediatric Society

President: Dr. G. R. Russell, 604 S. Cincinnati Ave., Tulsa.
Secretary: Dr. Luverne Hays, 108 W. 6th St., Tulsa.
Place: With Oklahoma State Medical Association. Time: Annual Meeting.

South Carolina Pediatric Society

President: Dr. George D. Johnson, Spartanburg.
Secretary-Treasurer: Dr. B. O. Ravenel, Roper Hospital, Charleston.

Texas Pediatric Society

President: Dr. Max Woodward, 202 N. Travis St., Sherman.
Secretary-Treasurer: Dr. John E. Ashby, 3610 Fairmount Ave., Dallas 4.
Place: Fort Worth. Time: Oct. 4-5, 1946.

Virginia Pediatric Society

President: Dr. Emily Gardner, 1100 W. Franklin St., Richmond 20.
Secretary: Dr. Louise Galvin, 214 S. Boulevard, Richmond 21.

West Virginia State Medical Society, Section on Pediatrics

President: Dr. Jack Basman, 1021 Quarrier St., Charleston.
Secretary: Dr. Harry E. Baldock, Medical Arts Bldg., Charleston.
Place: Huntington. Time: May 13-15, 1946.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. J. I. Hartman, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. Alexander N. Freed, 2012 W. 25th St., Cleveland.
Place: Cleveland Medical Library Bldg. Time: 8:15 p. m., October, December, February and April.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. J. H. Ebbs, 13 Queen's Park, Toronto, Canada.
Secretary: Dr. J. F. McCreary, 170 St. George St., Toronto, Canada.
Place: Academy of Medicine. Time: 8:30 p. m., third Thursday of each month.

Bronx Pediatric Society

President: Dr. Walter Levy, 12 E. 88th St., New York.
Secretary: Dr. Joseph Blasenstein, 960 Grand Concourse, New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Second Wednesday of each month, except June, July, August and September.

Brooklyn Academy of Pediatrics

President: Dr. Lambert Krahulik, 14 Sidney Pl., Brooklyn.
Secretary: Dr. Joseph Battaglia, 713 Bushwick Ave., Brooklyn 21.
Place: Granada Hotel. Time: 8:45 p. m., fourth Wednesday of February, March, April, May and November.

Buffalo Pediatric Society

President: Dr. Douglas P. Arnold, 159 Bidwell Parkway, Buffalo, N. Y.
Secretary: Dr. Richard A. Downey, 786 Forest Ave., Buffalo 9, N. Y.
Place: Children's Hospital, 219 Bryant St. Time: 8:30 p. m., first Monday of each month from September to June.

Central New York Pediatric Club

President: Dr. Arthur W. Benson, 2 St. Paul St., Troy.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Places: Various cities in New York. Time: Third Tuesday of April and October.

Chicago Pediatric Society

President: Dr. Louis W. Sauer, 636 Church St., Evanston, Ill.
Secretary: Dr. Henry G. Poncher, 1819 W. Polk St., Chicago 12.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May inclusive.

Cincinnati Pediatric Society

President: Dr. Theodore K. Selkirk, 3605 Edwards Rd., Cincinnati.
Secretary: Dr. John H. Hunt, Kemper Lane Bldg., Cincinnati 6.
Place: Children's Hospital, Elland Ave., Cincinnati. Time: On call.

Dallas Pediatric Society

President: Dr. O. René Caillet, 4325 Cole Ave., Dallas, Texas.
Secretary-Treasurer: Dorothy Wyvell, Bradford Memorial Hospital for Babies, Texas.
Place: Children's Medical Center. Time: 1 p. m., third Saturday and 8:30 p. m., the first Thursday of each month.

Detroit Pediatric Society

President: Dr. Otto Grob, 651 Fisher Bldg., Detroit 2, Mich.
Secretary: Dr. Harold B. Rothbart, 773 Fisher Bldg., Detroit 2, Mich.
Place: Variable. Time: Third Wednesday of each month.

Houston Pediatric Society

President: Dr. Raymond Cohen, 2300 Caroline St., Houston, Texas.
Secretary: Dr. Betty Moody, 526 Richmond Rd., Houston, Texas.
Place: River Oaks Country Club. Time: 7:30 p. m., fourth Monday of each month.

Kansas City (Missouri) Pediatric Society

President: Dr. Harry M. Gilkey, 1624 Professional Bldg., Kansas City.
Secretary: Dr. Leland Speer, 1022 Parkway, Kansas City.
Place: Kansas City General Hospital. Time: On call.

Los Angeles County Medical Association, Pediatric Section

President: Dr. Albert L. Hill, 1401 S. Hope St., Los Angeles.
Secretary-Treasurer: Dr. Robert Simonds, 267 S. Beverly Dr., Beverly Hills, Calif.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd. Time: Second Monday of February, April, June, October and December.

Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Henry Rascoff, 895 Eastern Parkway, Brooklyn.
Secretary: Dr. Harold Levy, 750 St. Marks Ave., Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: 9:00 p. m., fourth Monday of each month.

Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. Meyeron Coe, 217-02-91st Ave., Queens Village, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144-38th Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

Medical Society of the District of Columbia, Section on Pediatrics

President: Dr. John Washington, 2203 Wyoming Ave., Washington, D. C.
Secretary-Treasurer: Dr. George Maksim, 1418 Good Hope Rd. S.E., Washington, D. C.
Place: Medical Society Bldg., 1718 M St. N. W. Time: 8 p. m., third Thursday of October, January, March and May.

Memphis Pediatric Society

President: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Barton Etter, 1024 Madison Ave., Memphis, Tenn.
Place: Memphis Country Club. Time: 8 p. m., Dec. 13, 1946.

Milwaukee Pediatric Society

President: Dr. G. H. Fellman, 231 W. Wisconsin Ave., Milwaukee.
Secretary-Treasurer: Dr. R. P. Showalter, 411 E. Mason St., Milwaukee 2.
Place: Milwaukee Children's Hospital. Time: Second Wednesday in February, April, June, October and December.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Robert O. Du Bois, 122 E. 76th St., New York.
Secretary: Dr. Harold W. Dargeon, 1095 Park Ave., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from November to May, inclusive, 8:30 p. m.

Oklahoma City Pediatric Society

President: Dr. William M. Taylor, 625½ N. W. 10th St., Oklahoma City.
Secretary: Dr. Jeanne McKinnon-Shofstall, 1019 N. Lee St., Oklahoma City.
Place: Oklahoma Club. Time: Third Thursday of each month.

Philadelphia Pediatric Society

President: Dr. Waldo E. Nelson, Temple University School of Medicine, Philadelphia.
Secretary: Dr. Sherman Little, 1740 Bainbridge St., Philadelphia 46.
Place: College of Physicians, 19 S. 22d St. Time: 8:30 p. m., second Tuesday in October, December, February and April.

Pittsburgh Pediatric Society

President: Dr. Elwood Stitzel, 403 Central Trust Bldg., Altoona, Pa.
Secretary-Treasurer: Dr. C. J. Stoecklein, Medical Arts Bldg., Pittsburgh 13.
Place: Pittsburgh Academy of Medicine. Time: Second Friday in October, December, February and April.

Richmond Pediatric Society

President: Dr. Edwin L. Kendig Jr., 828 W. Franklin St., Richmond 20, Va.
Secretary-Treasurer: Dr. Thomas S. Chalkley, 1200 E. Broad St., Richmond, Va.
Place: Medical College Hospital. Time: 8 p. m., third Thursday of each month, except June, July and August.

Rochester Pediatric Society

President: Dr. William L. Bradford, 260 Crittenden Blvd., Rochester 7, N. Y.
Secretary-Treasurer: Dr. Donald D. Posson, 222 Chili Ave., Rochester 11, N. Y.
Place: Rochester Academy of Medicine or arrangement by program committee.
Time: Third Friday of each month from October to May.

St. Louis Pediatric Society

President: Dr. Joseph C. Jaudon, 337 N. Euclid Ave., St. Louis.
Secretary-Treasurer: Dr. Gilbert B. Forbes, 500 S. Kingshighway, St. Louis 10.
Time: Second Thursday of each month from October to May, inclusive.

Seattle Pediatric Society

President: Dr. D. M. Dayton, 740 St. Helens Ave., Tacoma.
Secretary: Dr. W. B. Chesley, 1306 Madison St., Seattle 4.
Place: College Club. Time: Third Friday of each month from September to June at 6:30 p. m.

Southwestern Pediatric Society

President: Dr. Robert J. Dostal, 710 Wilshire Blvd., Santa Monica, Calif.
Secretary: Dr. H. M. Van Dyke, 541 E. Broadway, Long Beach, Calif.
Place: University Club of Los Angeles. Time: 6:30 p. m., first Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Park Bradshaw, Muskegon, Mich.
Secretary: Dr. Harry A. Towsley, 1313 E. Ann St., Ann Arbor, Mich.
Place: University Hospital, Ann Arbor, Mich. Time: Oct. 25-26, 1946.

Westchester County Medical Society, Pediatrics Section (New York)

President: Dr. John B. Ahouse, 27 Ludlow St., Yonkers, N. Y.
Secretary-Treasurer: Dr. Elvira Ostlund, 64 Highland Rd., Rye, N. Y.
Place: Hospitals of Westchester County. Time: Third Thursday in November, January, March and May.